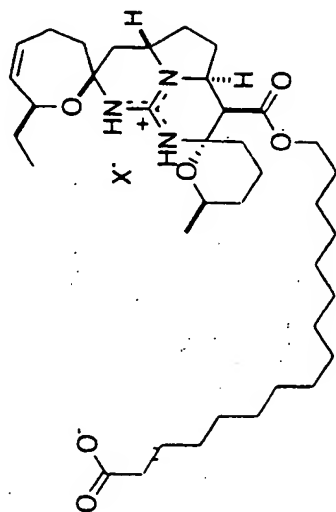
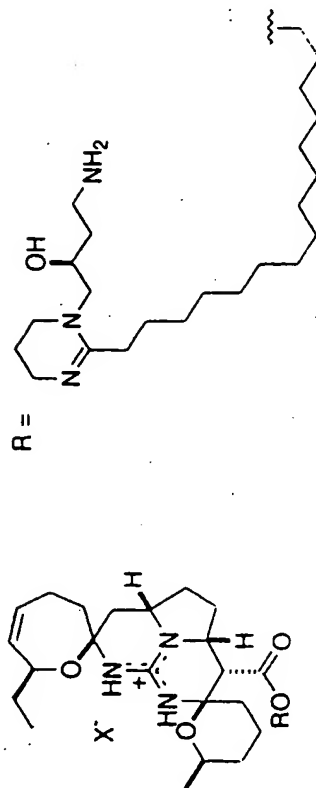


pilomycin A (1, $R^1 = R^2 = R^3 = H$; $n = 1$)
 crambescidin 800 (2, $R^1 = R^3 = H$, $R^2 = OH$; $n = 1$)
 crambescidin 816 (3, $R^1 = R^2 = OH$, $R^3 = H$; $n = 1$)
 crambescidin 830 (4, $R^1 = R^2 = OH$, $R^3 = H$; $n = 2$)
 crambescidin 844 (5, $R^1 = R^2 = OH$, $R^3 = H$; $n = 3$)
 celeromycin (6, $R^1 = R^2 = H$, $R^3 = OH$; $n = 1$)

13, 14, 15 - isocrambescidin 800 (10)



13, 14, 15 - isocrambescidin 657 (10a)



fromiamycin (9)

$R = H$ (7)
 $R = allyl$ (8)

Figure 1

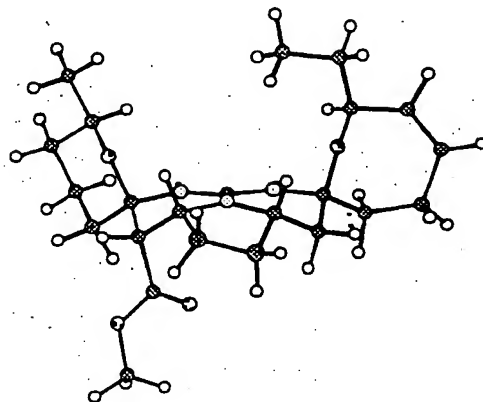


Figure 2

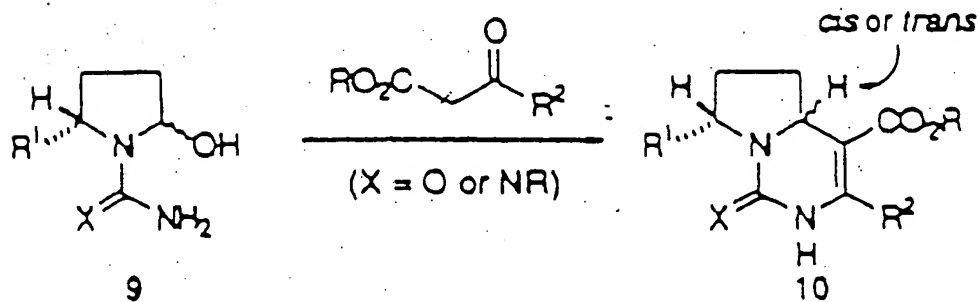
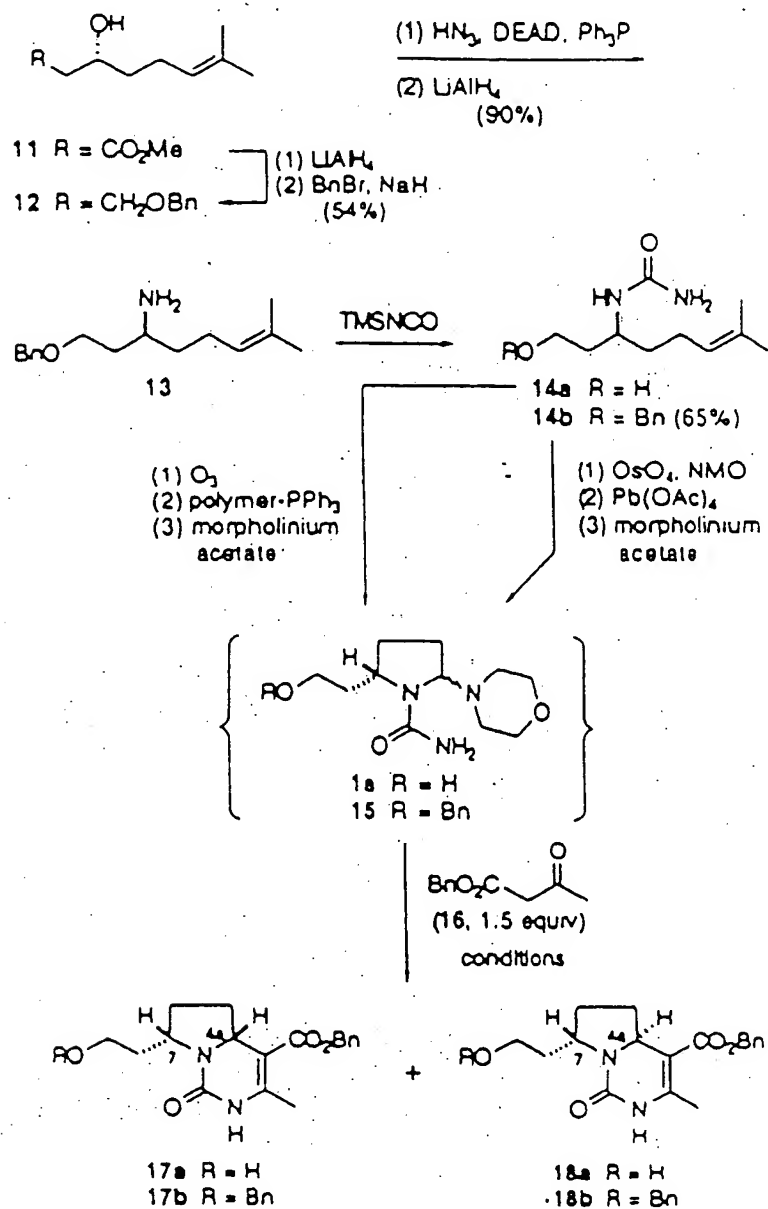


FIGURE . 3



substrate	reaction conditions	17:18 (yield) ^a
1a	morpholinium acetate (1.5 eq), $\text{CF}_3\text{CH}_2\text{OH}$, 60 °C, 48 h	4:1 (80%)
15		4:1 (81%)
15	PPE, CH_2Cl_2 , 23 °C, 48 h	1:4 (60%)

^a Combined overall yield of 17 and 18 from 14.

FIGURE 4

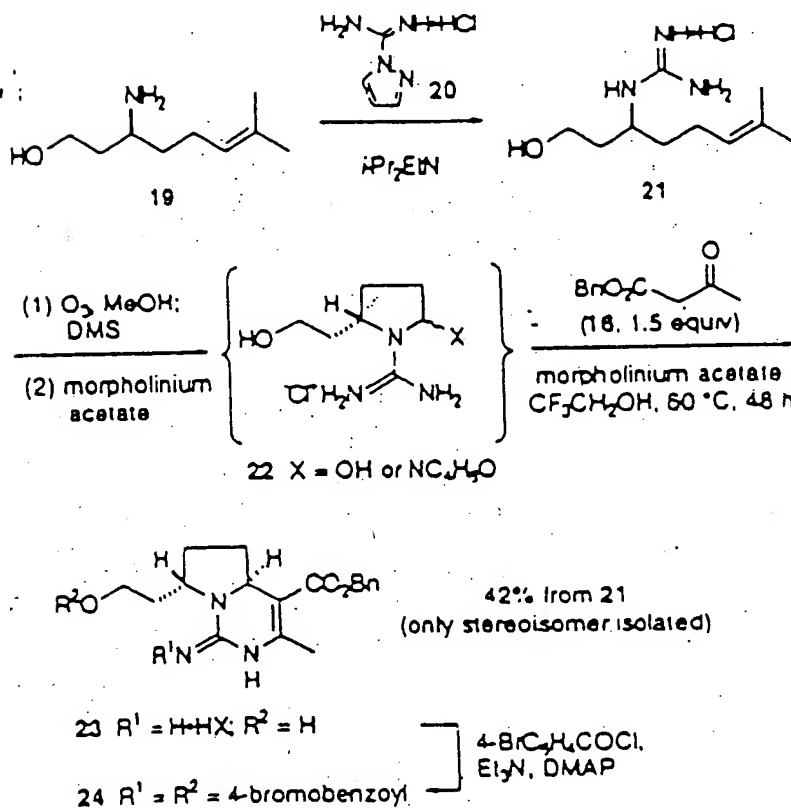
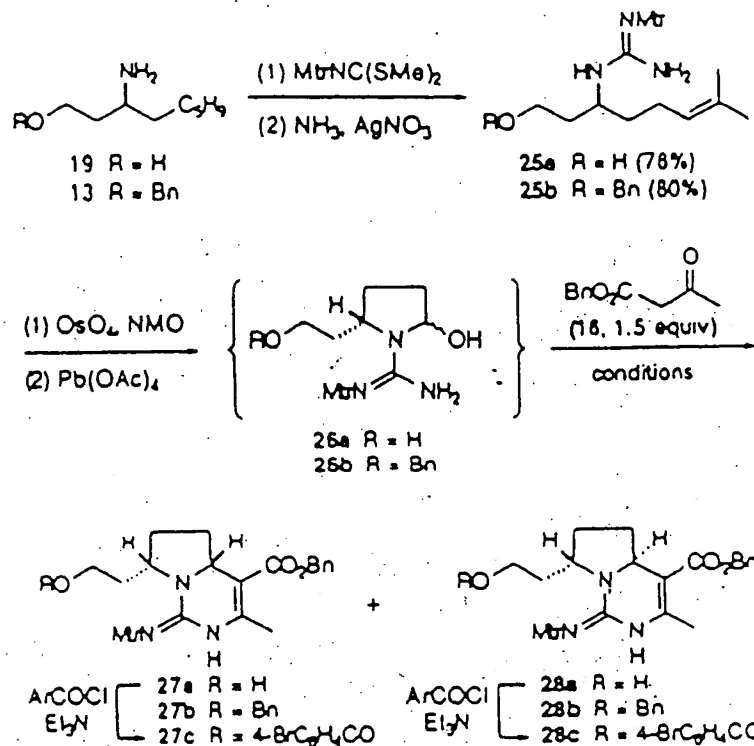


FIGURE 5



substrate	reaction conditions	27:28 (yield) ^a
25a	morpholinium acetate (1.5 eq),	6:1 (61%)
25b	CF ₃ CH ₂ OH, 60 °C, 48 h	7:1 (84%)
25b	PPE, CH ₂ Cl ₂ , 23 °C, 48 h	1:20 (61%)

^a Combined overall yield of 27 and 28 from 25.

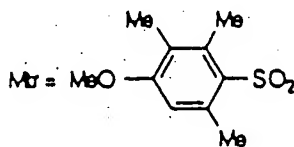


FIGURE 6

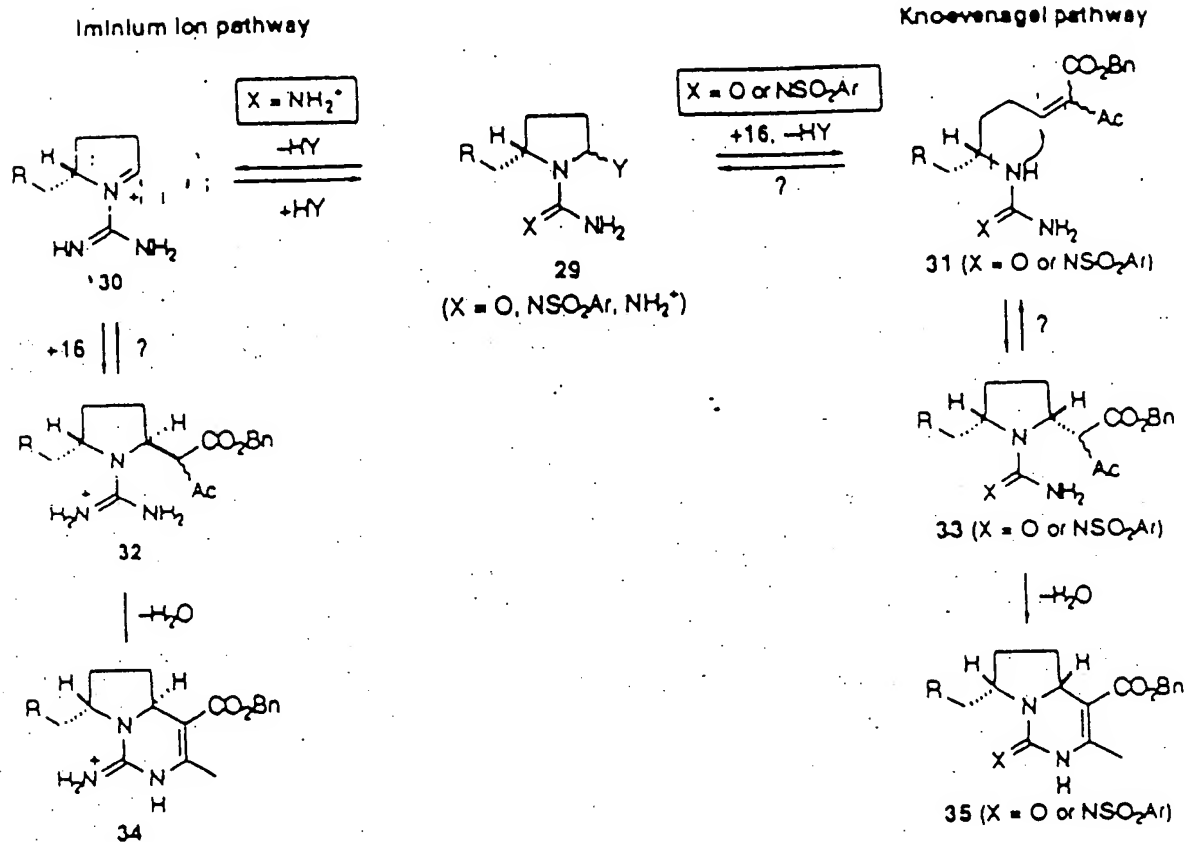


FIGURE 7

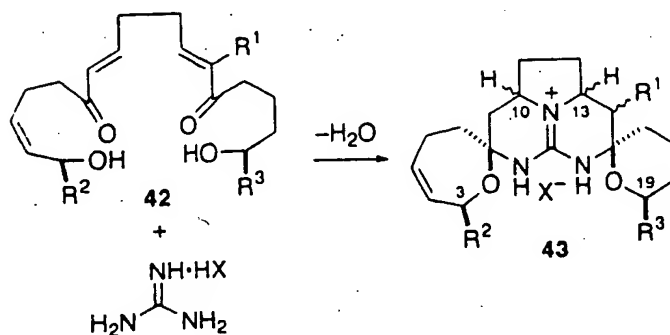
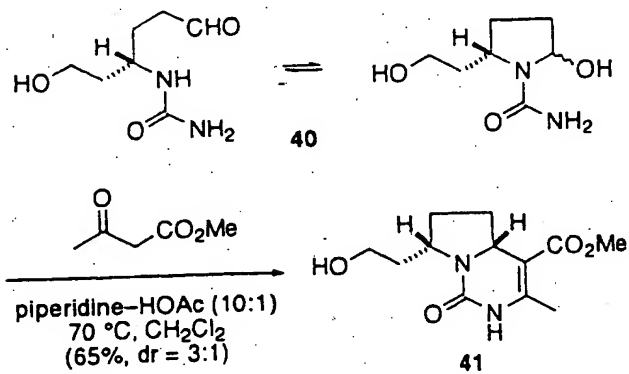
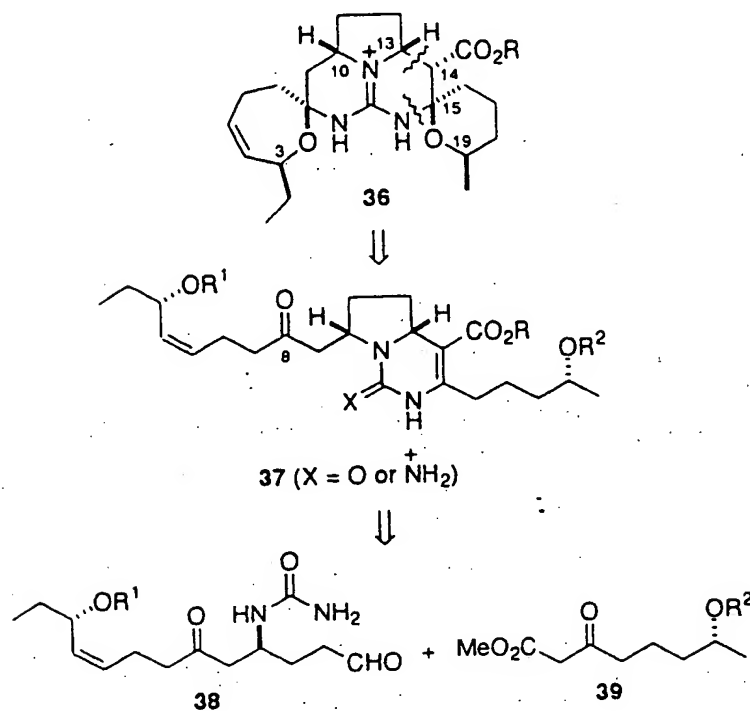


Figure 8

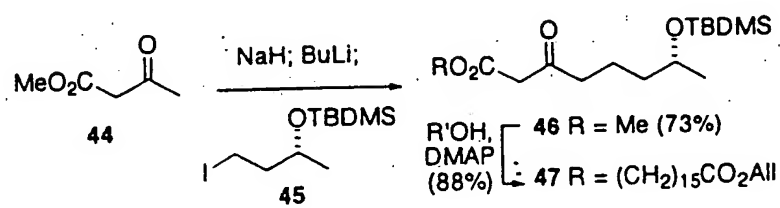


Figure 9

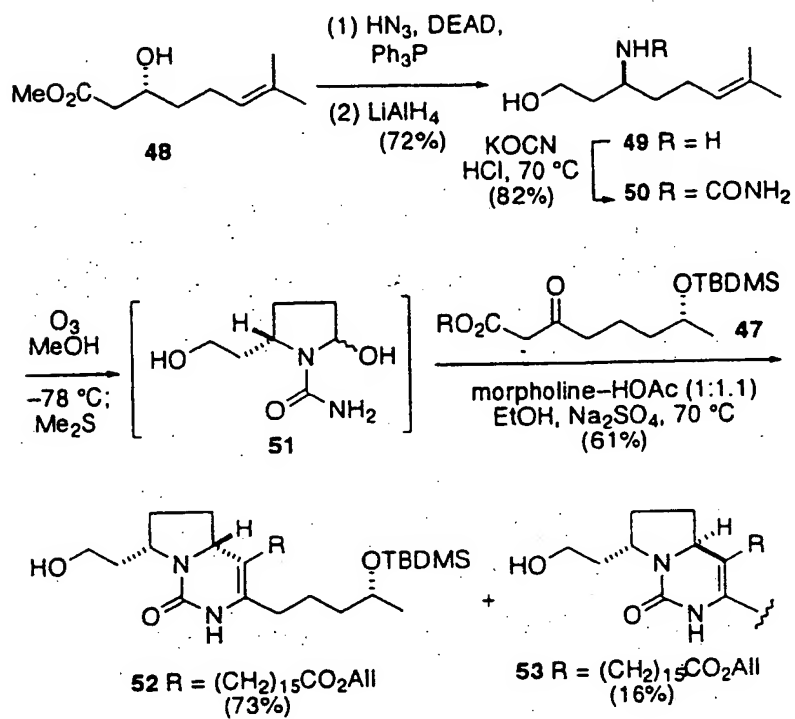


Figure 10

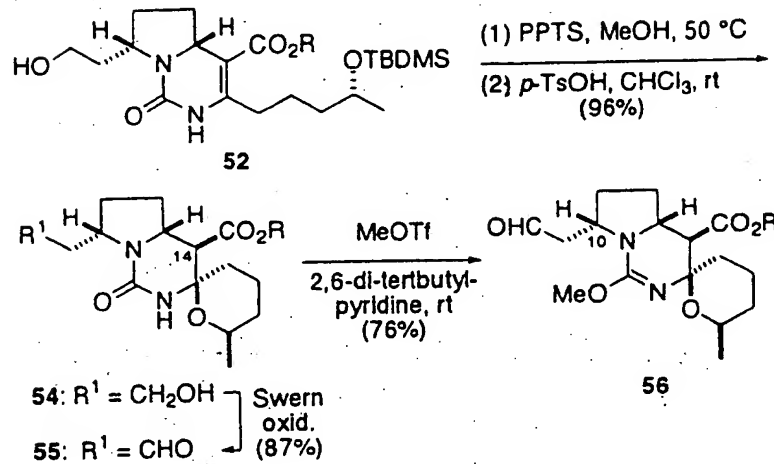


Figure 11

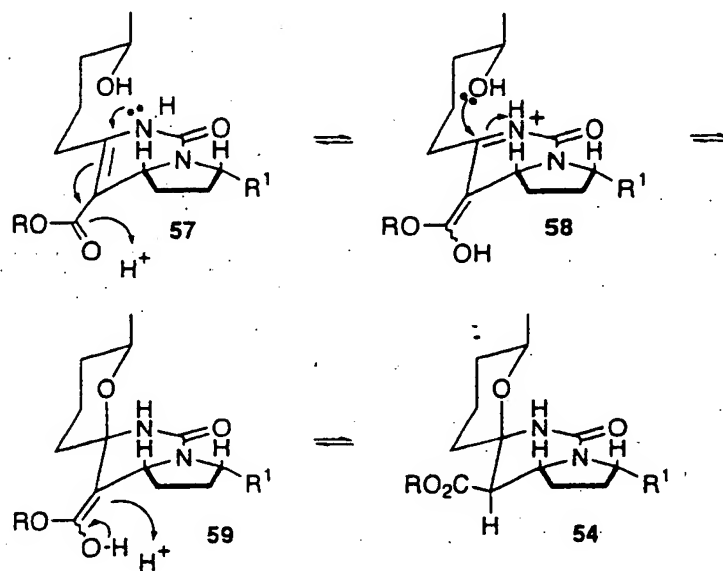


Figure 12

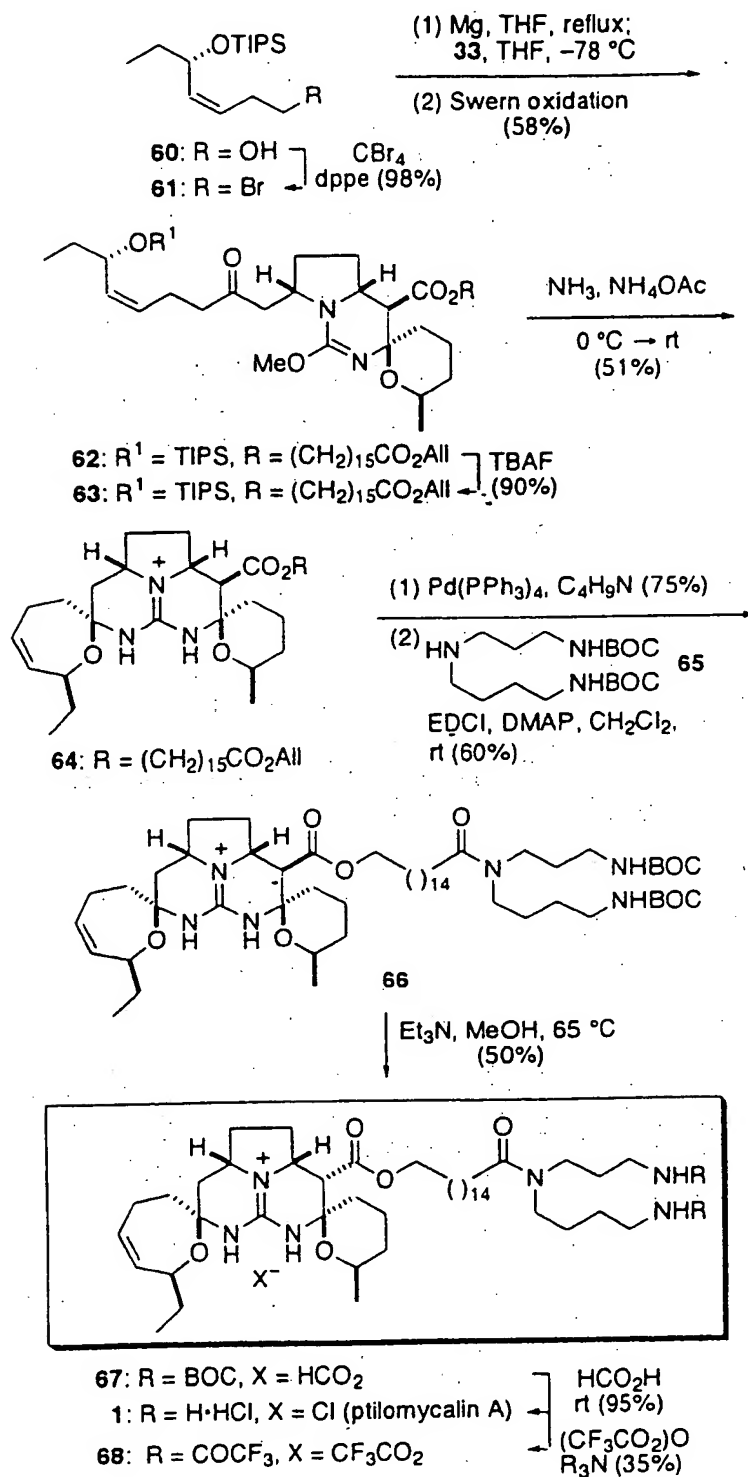


Figure 13

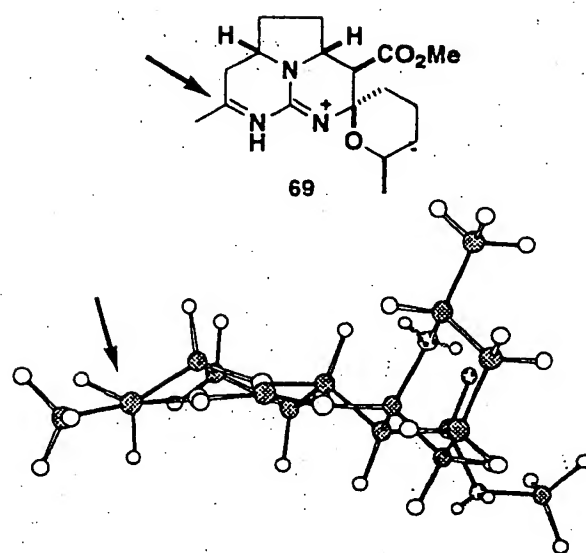


Figure 14

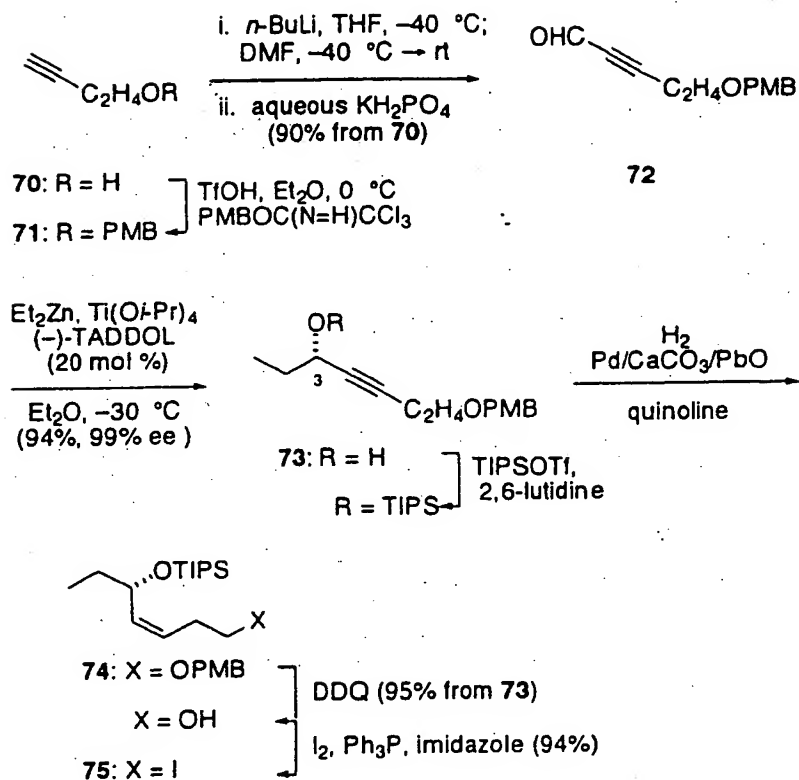


Figure 15

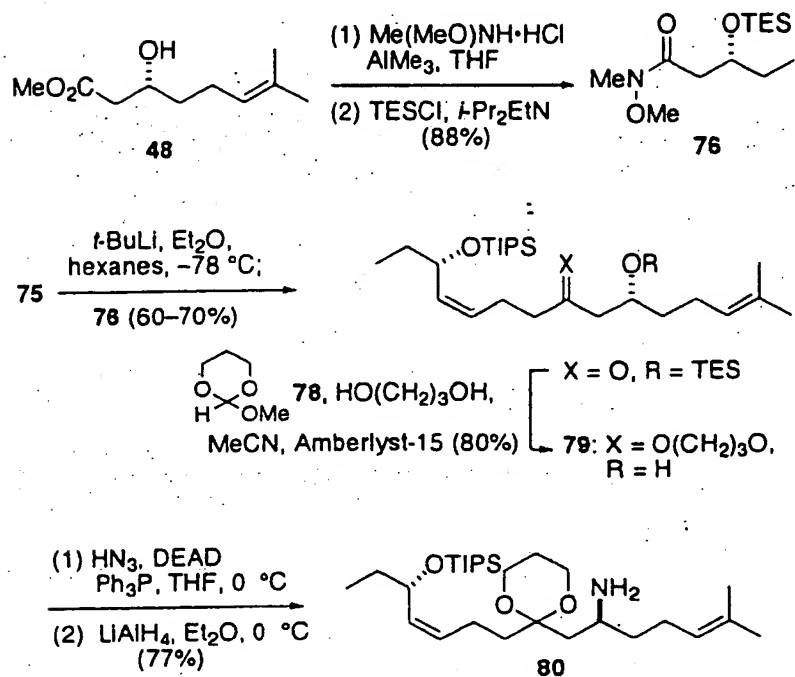


Figure 16

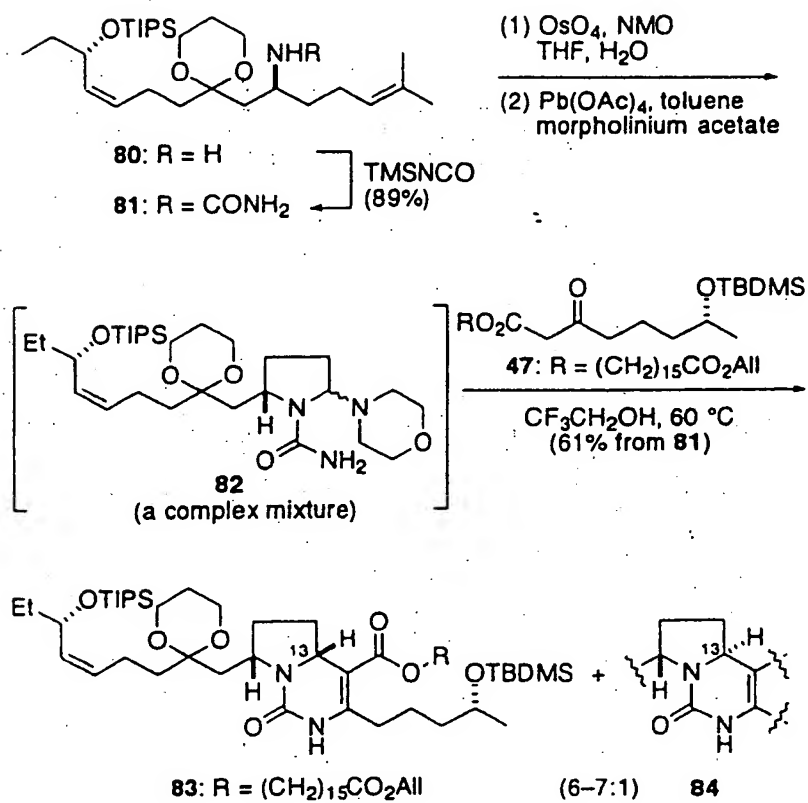


Figure 17

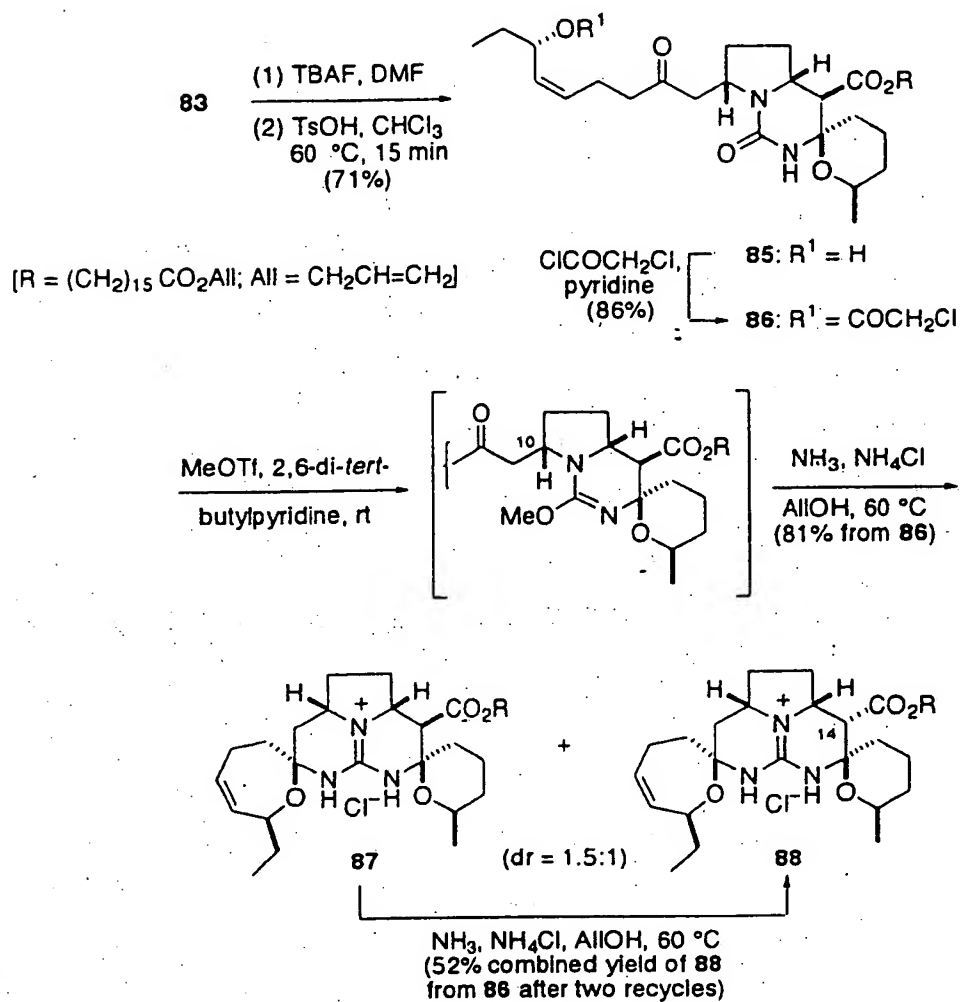
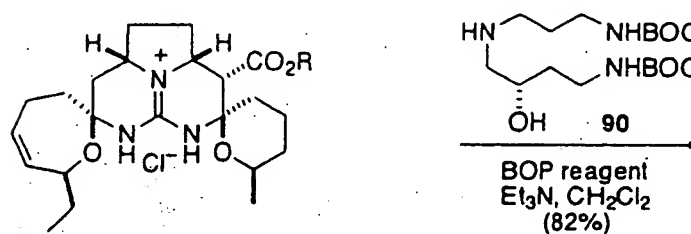
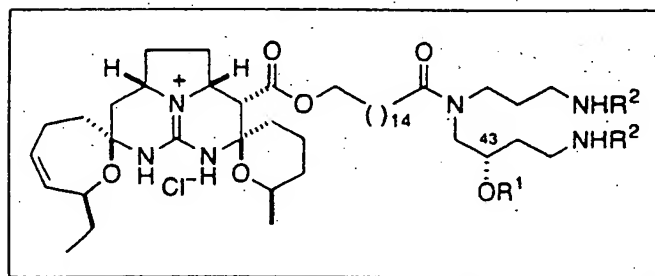


Figure 18



88: $\text{R} = (\text{CH}_2)_{15} \text{CO}_2\text{All}$
 89: $\text{R} = (\text{CH}_2)_{15} \text{CO}_2\text{H}$

Reaction conditions: $\text{Pd}(\text{Ph}_3\text{P})_4$, morpholine (94%)



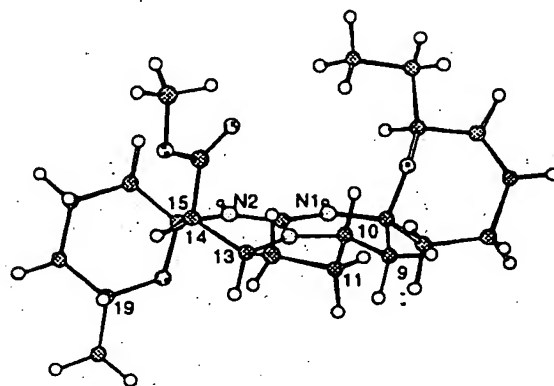
3 M HCl
 EtOAc (75%)

(R)-MTPA-Cl
 Et_3N , CH_2Cl_2

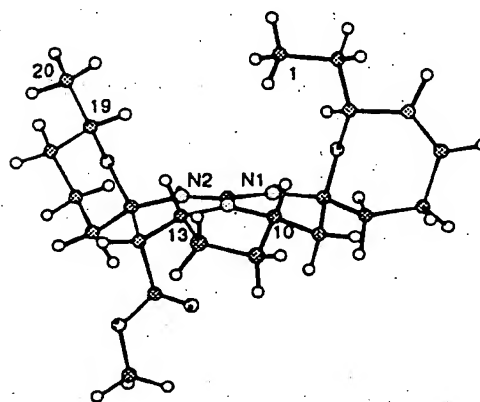
91: $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{BOC}$
 2: $\text{R}^1 = \text{H}$, $\text{R}^2 = \text{H} \cdot \text{HCl}$ (crambescidin 800)
 92: $\text{R}^1 = \text{R}^2 = \text{Ac}$
 93: $\text{R}^1 = \text{R}^2 = (\text{S})\text{-COC}(\text{CF}_3)(\text{OMe})\text{Ph}$

Reaction conditions: Ac_2O , pyridine (35%)

Figure 19



13,14,15-isocrambescidin core



crambescidin/ptilomycalin A core

Figure 20

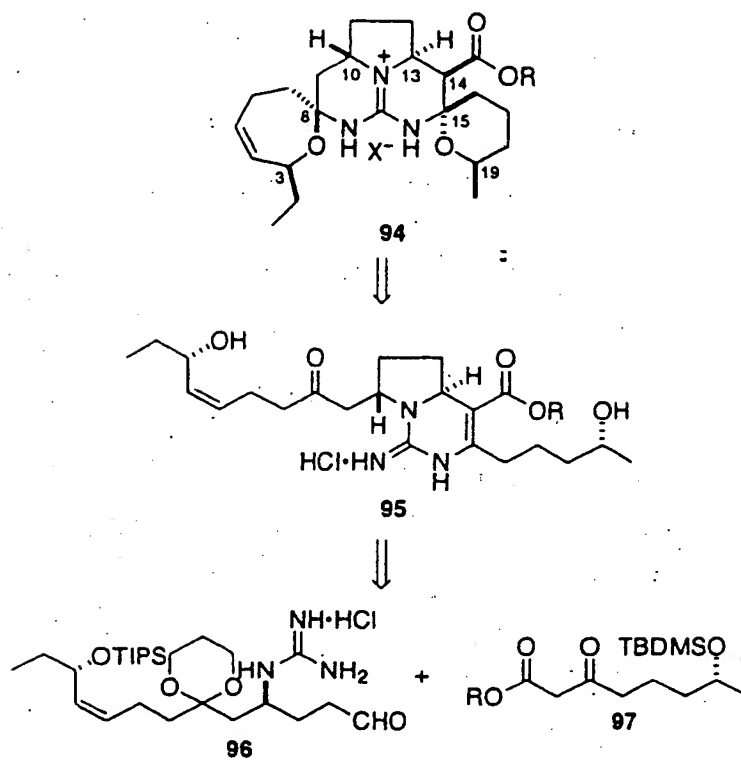


Figure 21

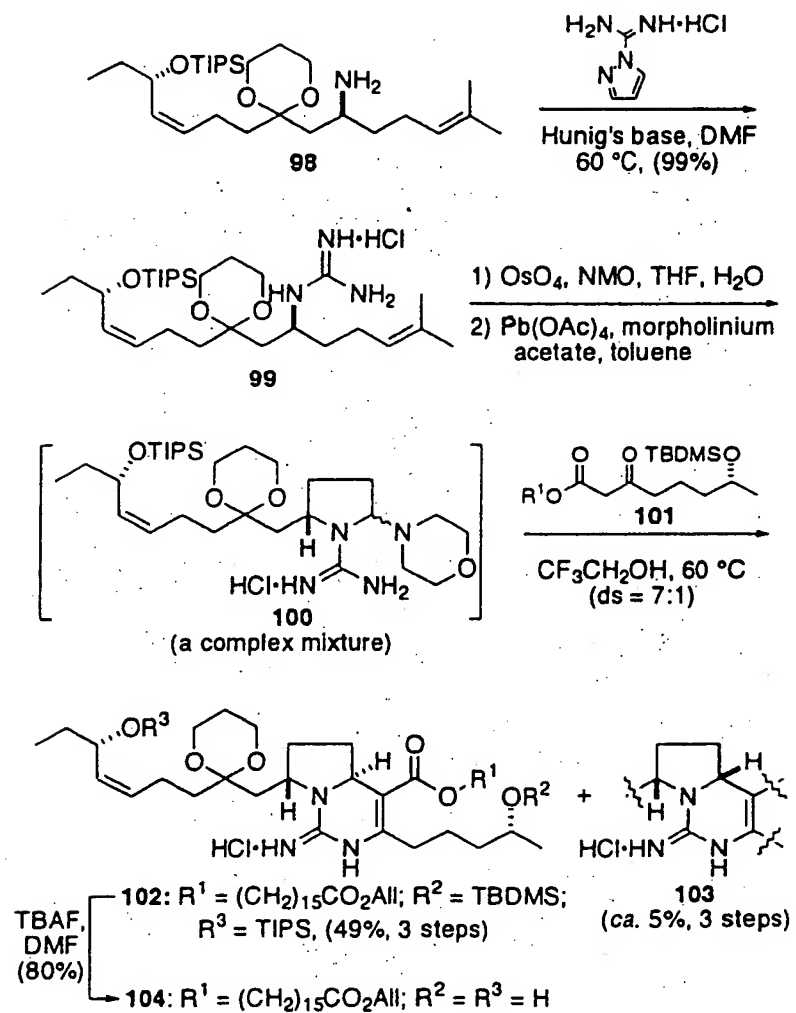


Figure 22

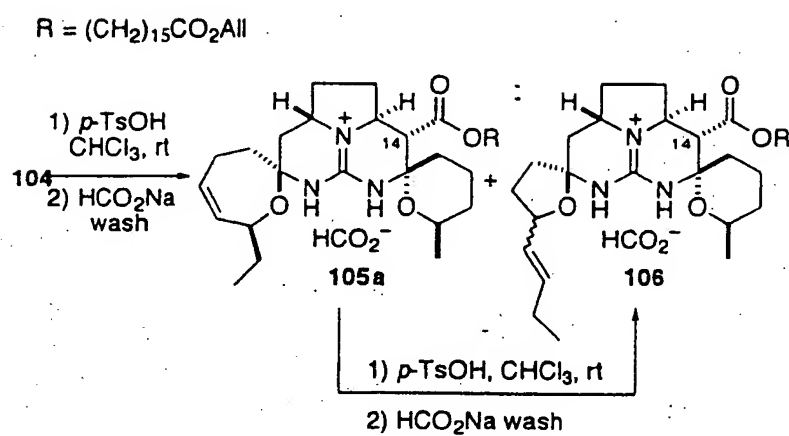


Figure 23

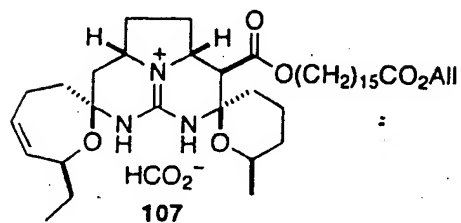
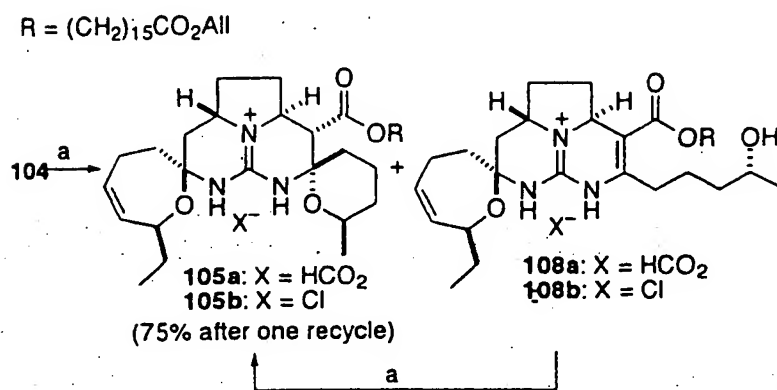


Figure 24



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂ Na wash
or 0.1 N HCl wash

Figure 25

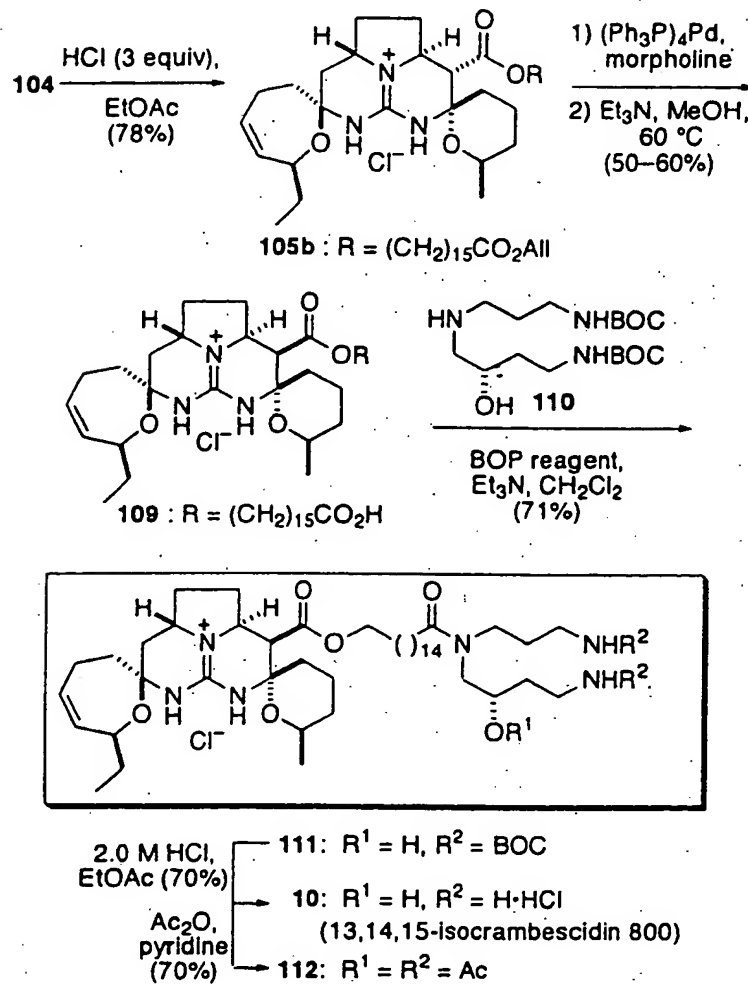


Figure 26



Figure 27

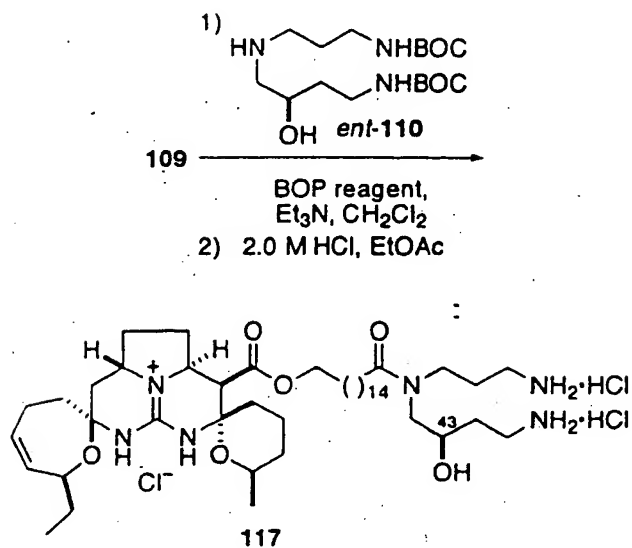


Figure 28

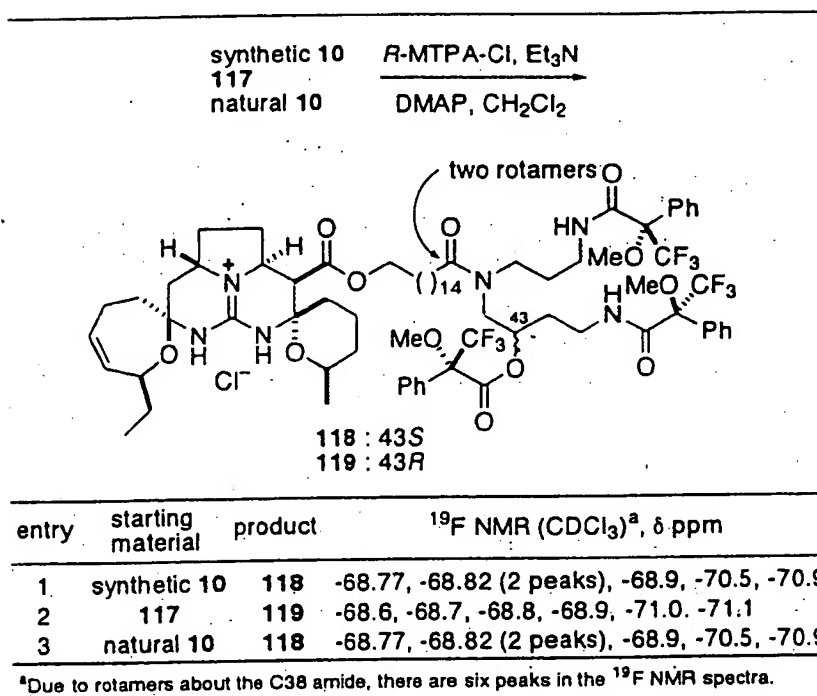


Figure 29

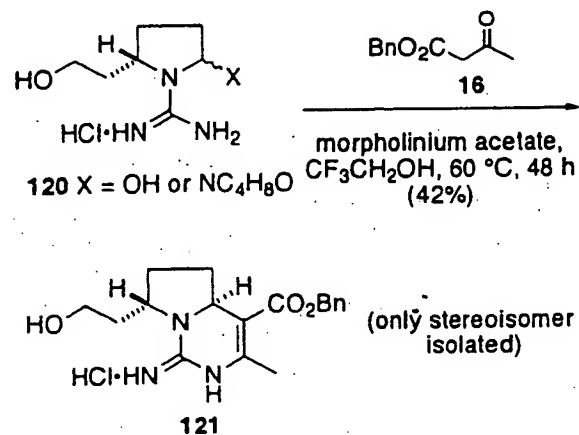


Figure 30

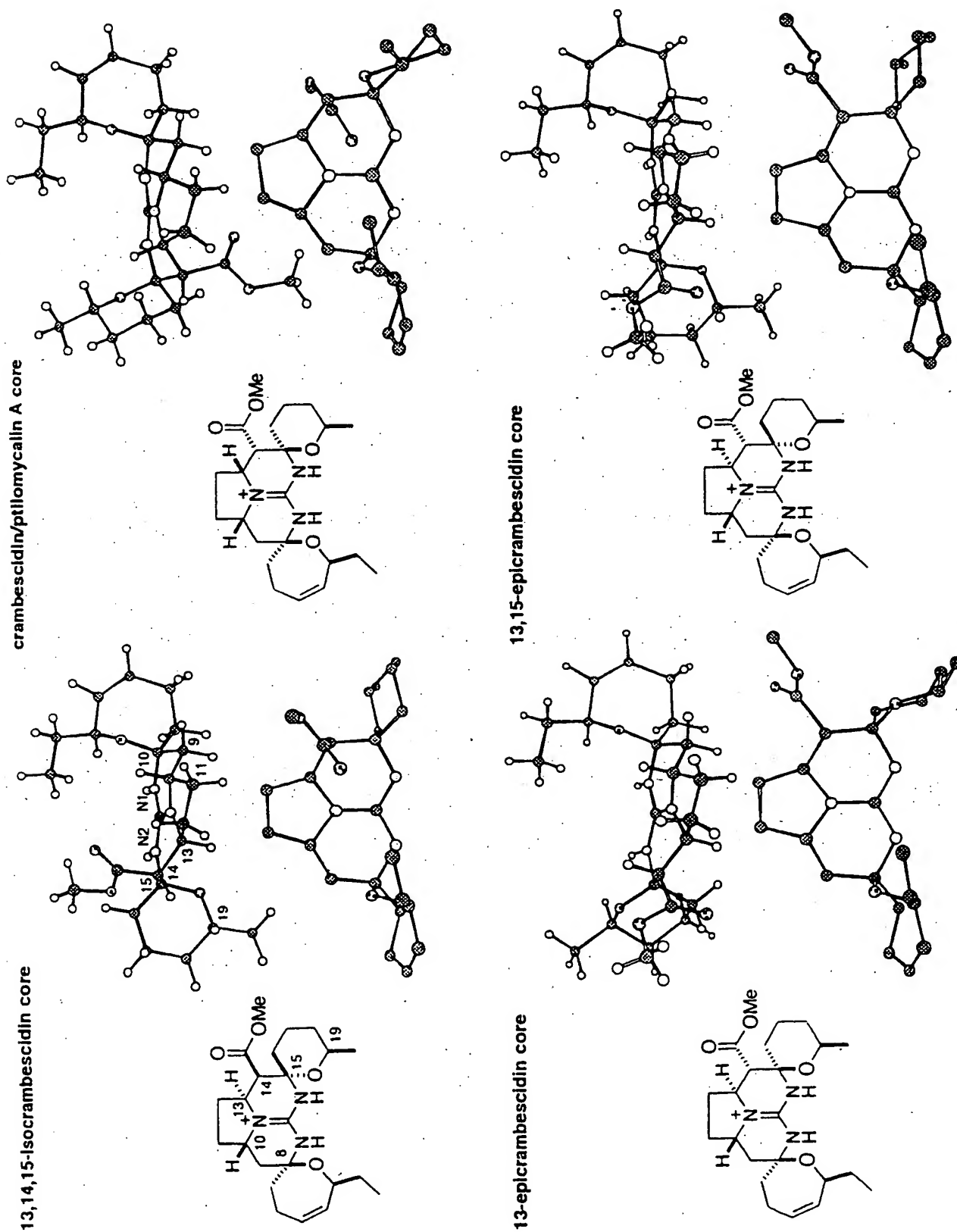


Figure 31

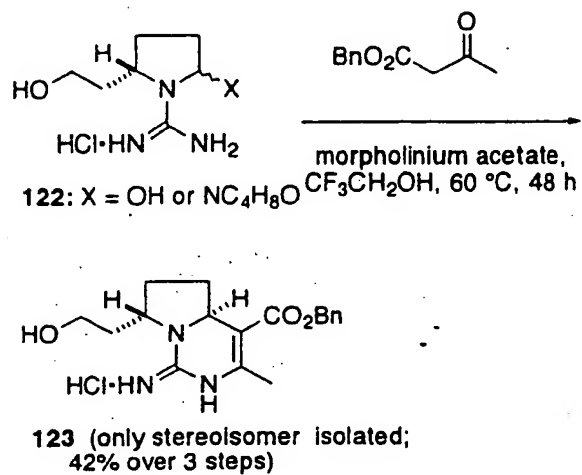


Figure 32

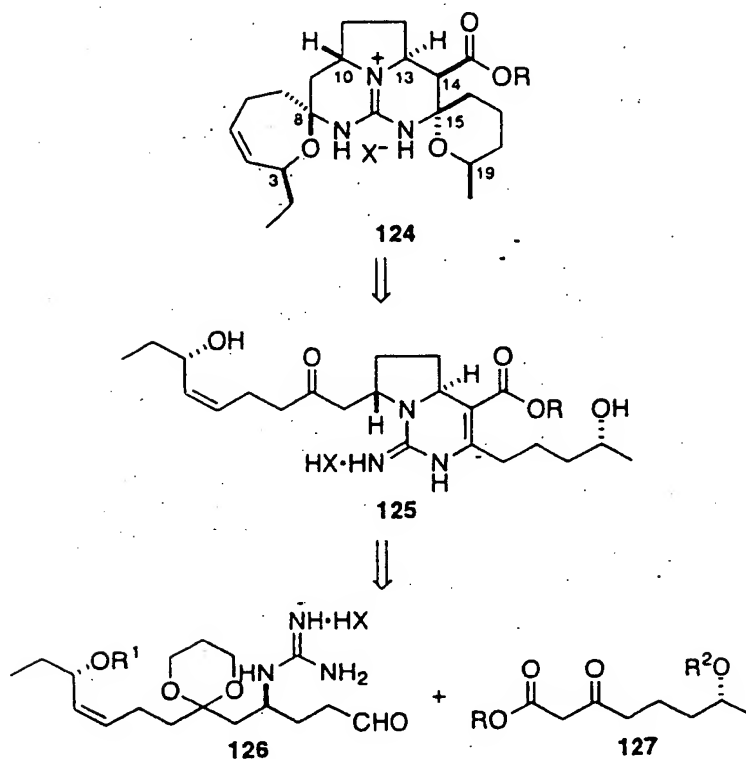


Figure 33

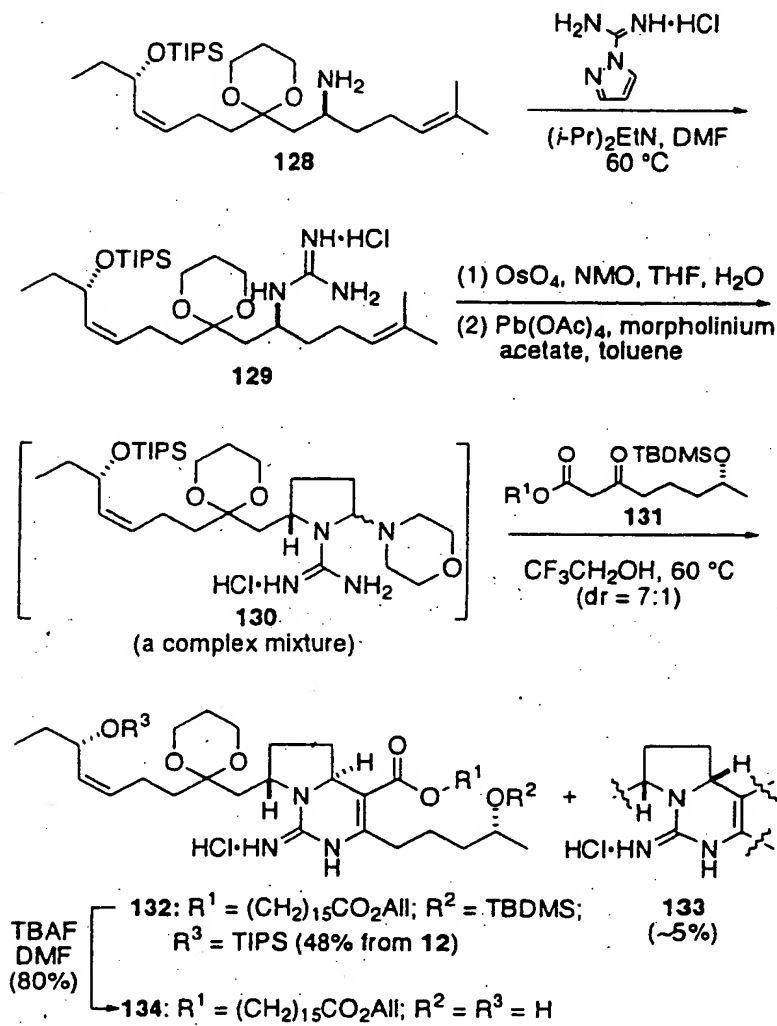


Figure 34

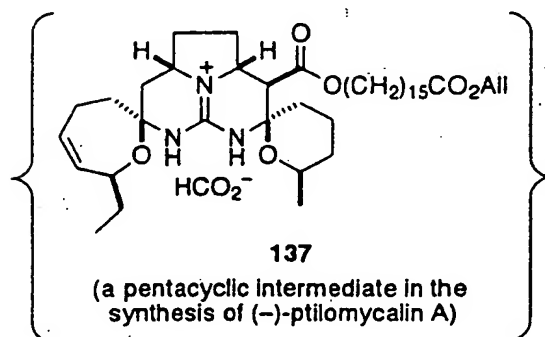
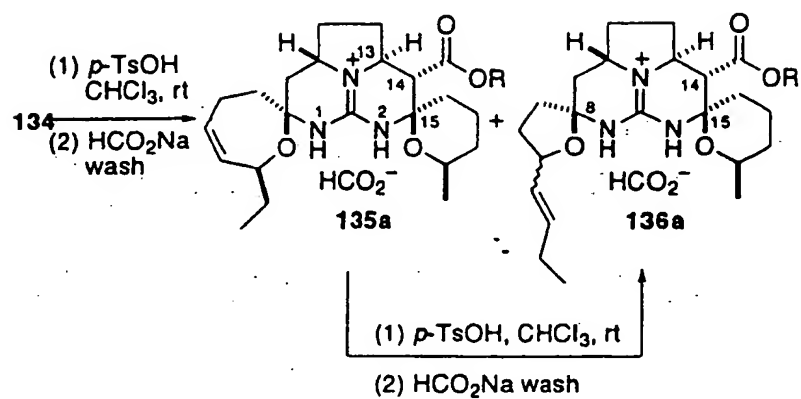
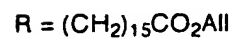
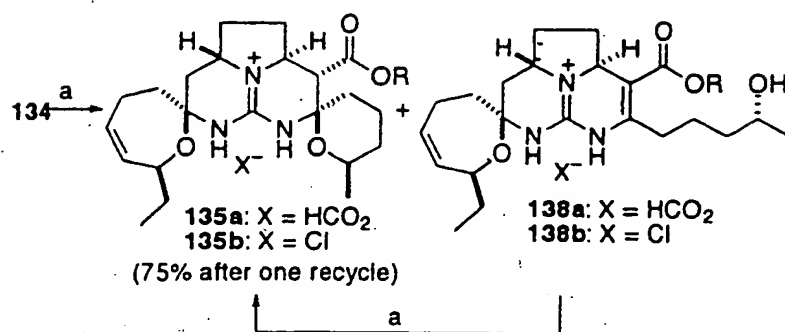


Figure 35

R = (CH₂)₁₅CO₂AlI



^aReagents: (a) PPTS, CHCl₃, 90 °C, 24 h; HCO₂Na wash
or 0.1 N HCl wash

Figure 36

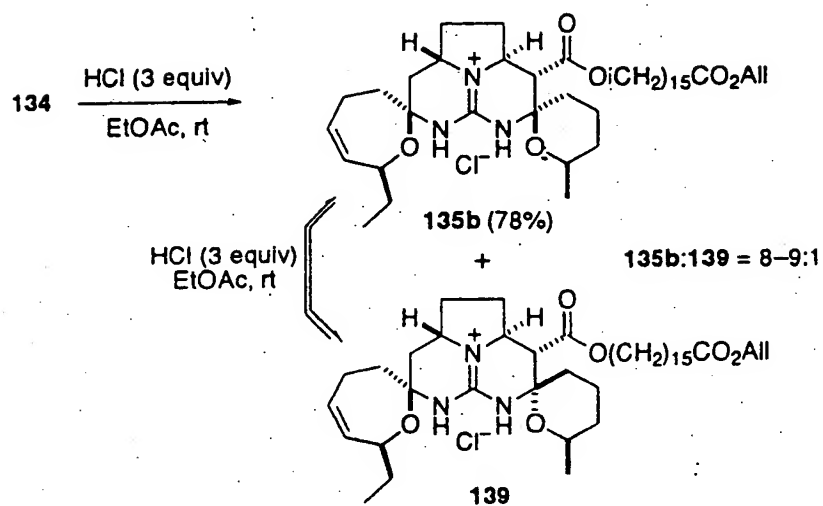


Figure 37

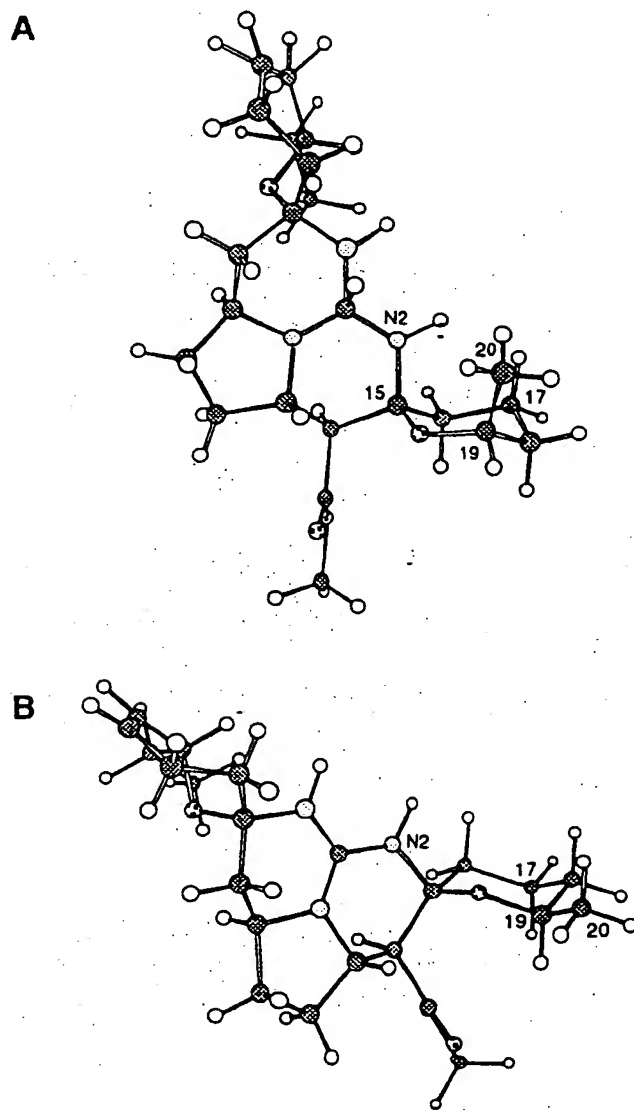


Figure 38

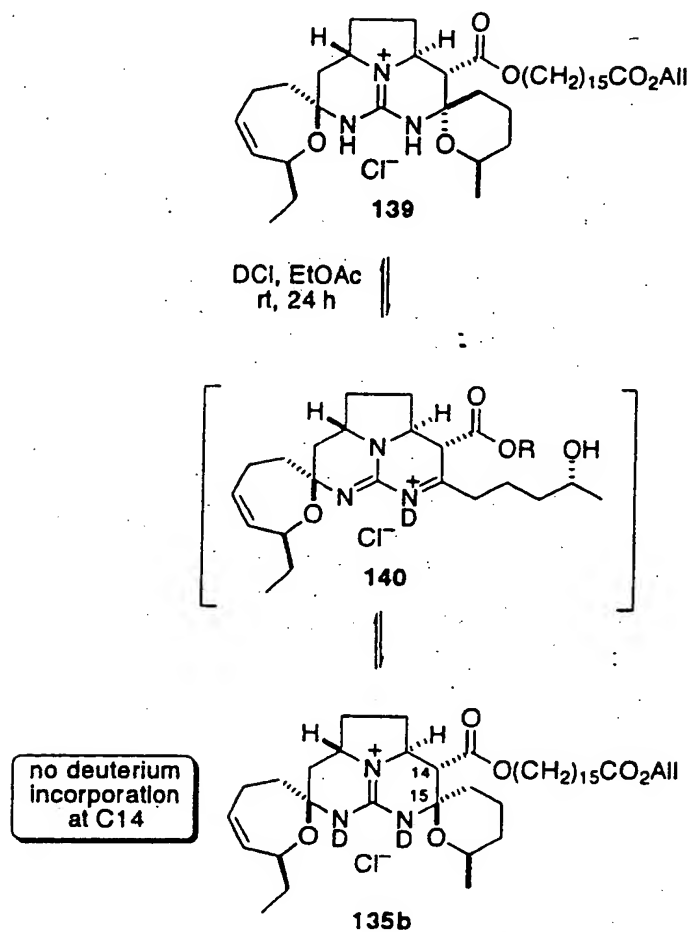


Figure 39

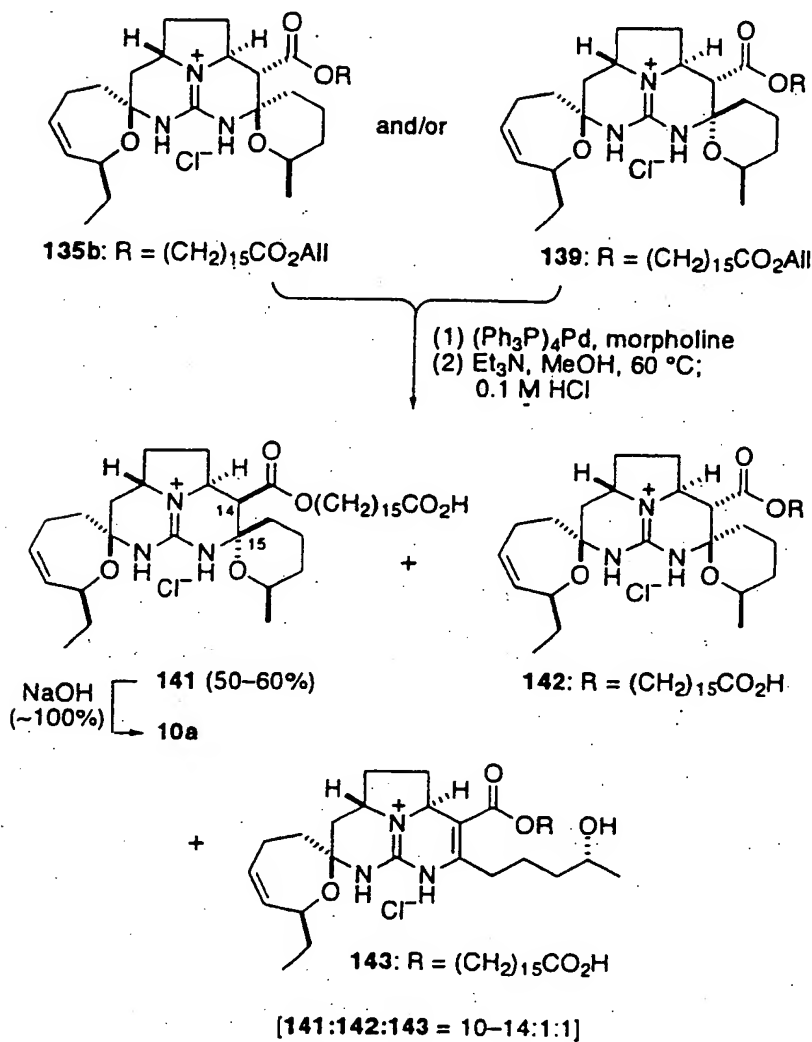


Figure 40

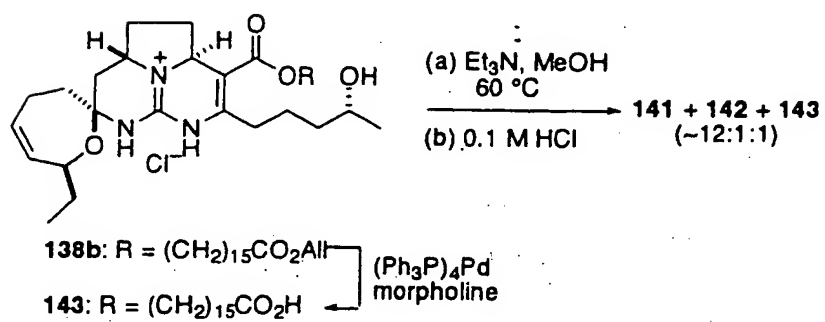


Figure 41

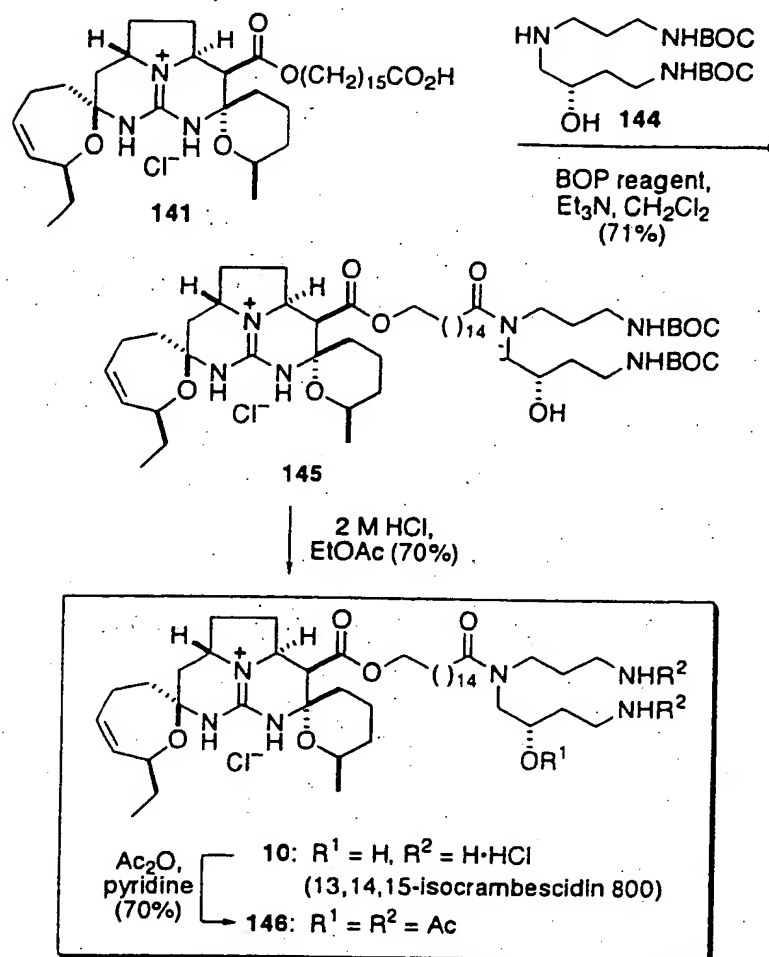


Figure 42

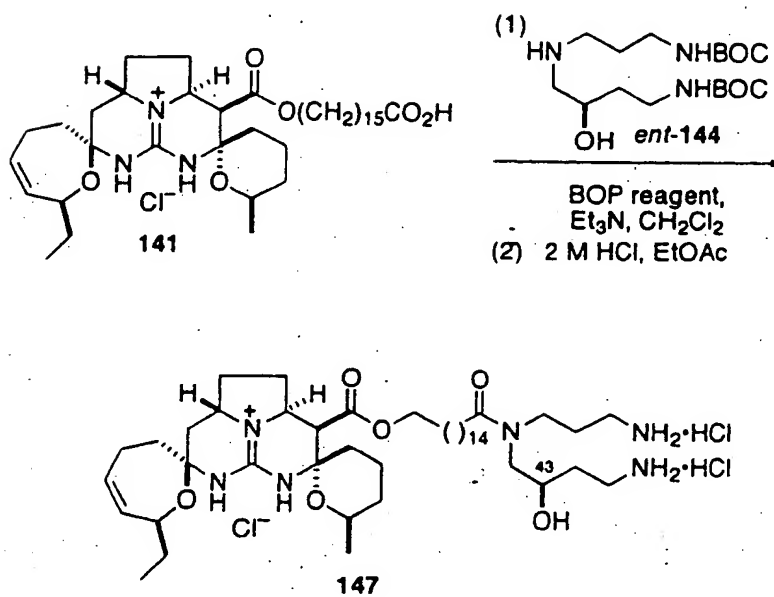
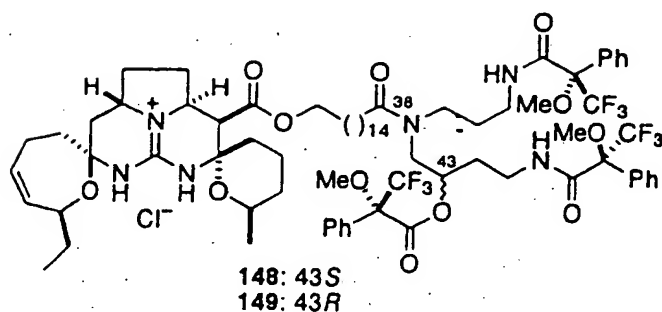


Figure 43



entry	starting material	product	^{19}F NMR (CDCl_3) ^a , δ ppm
1	synthetic 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9
2	147	149	-68.6, -68.7, -68.8, -68.9, -71.0, -71.1
3	natural 10	148	-68.77, -68.82 (2 peaks), -68.9, -70.5, -70.9

^aDue to rotamers about the C38 amide bond on the NMR time scale, six peaks are observed in the ^{19}F NMR spectra.

Figure 44

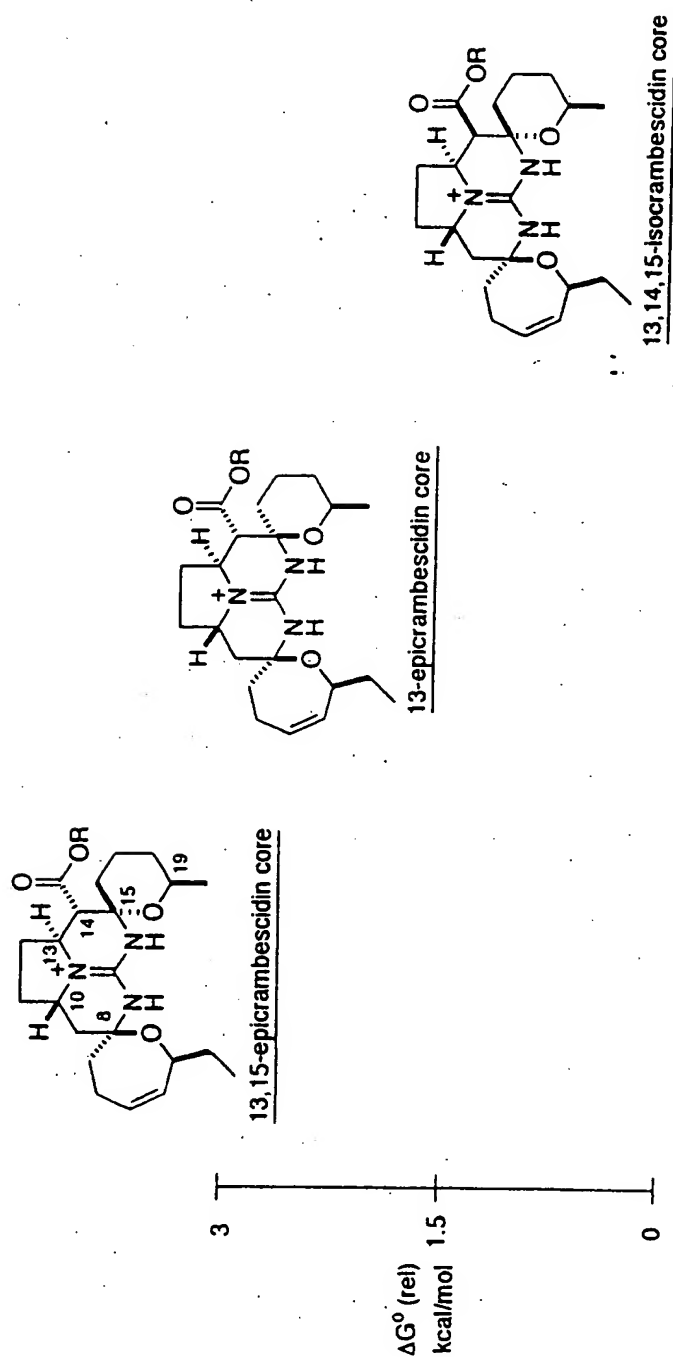


Figure 45

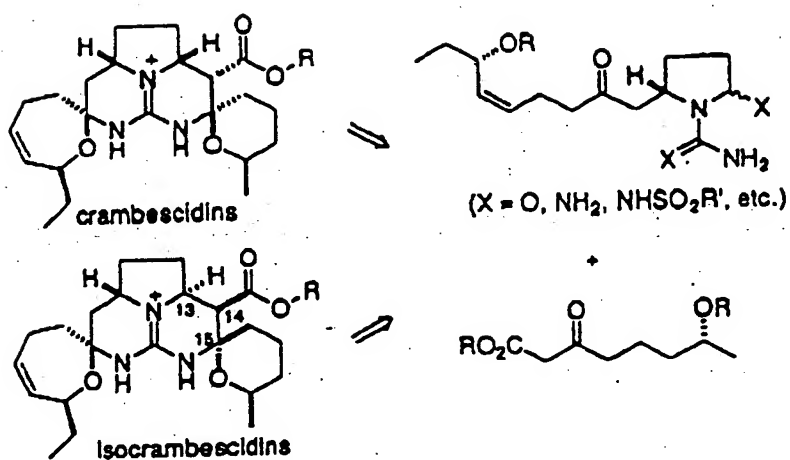


Figure 46

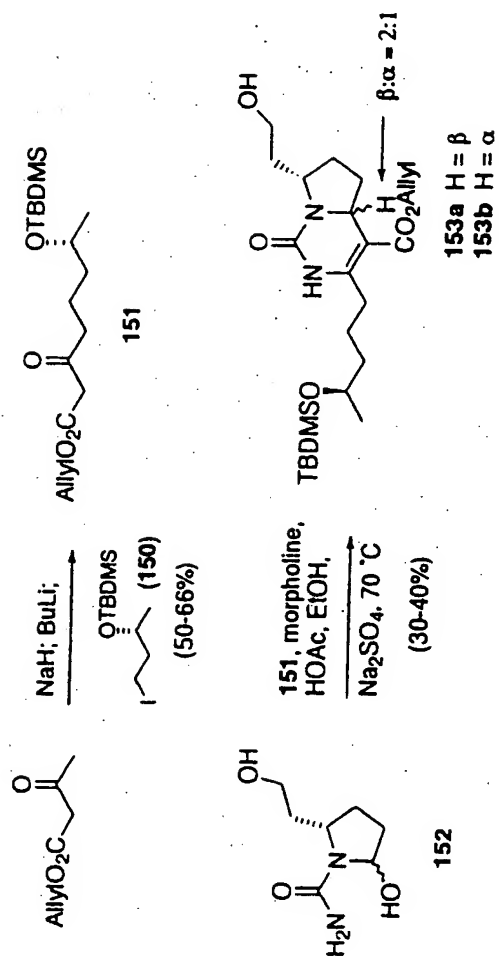


Figure 47

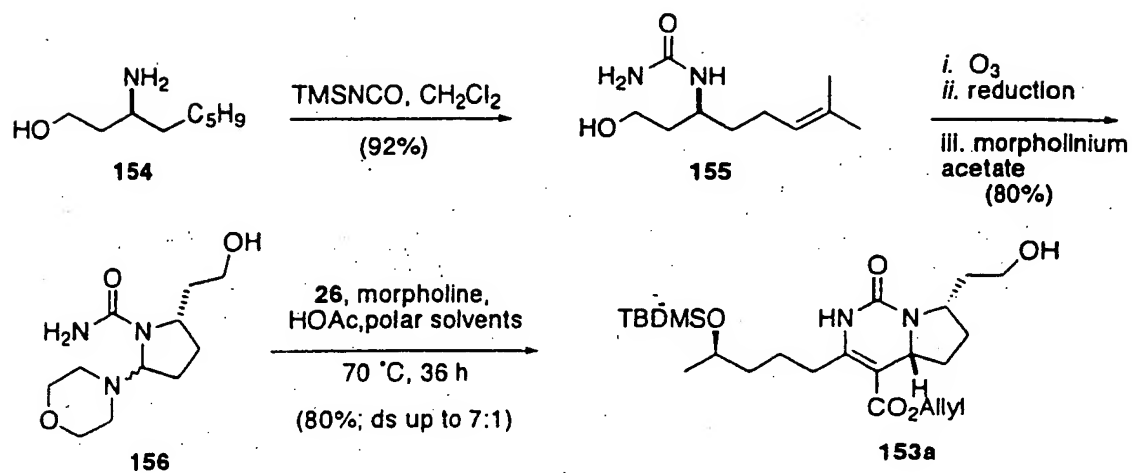


Figure 48

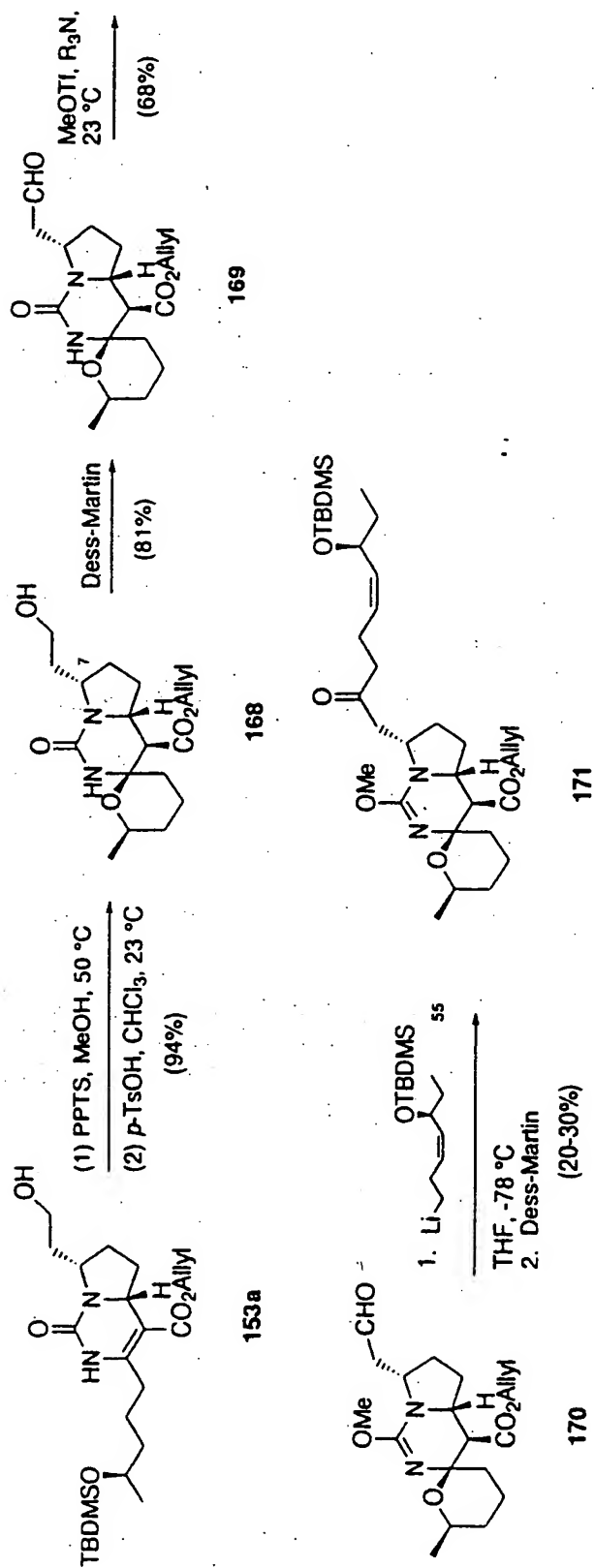


Figure 50

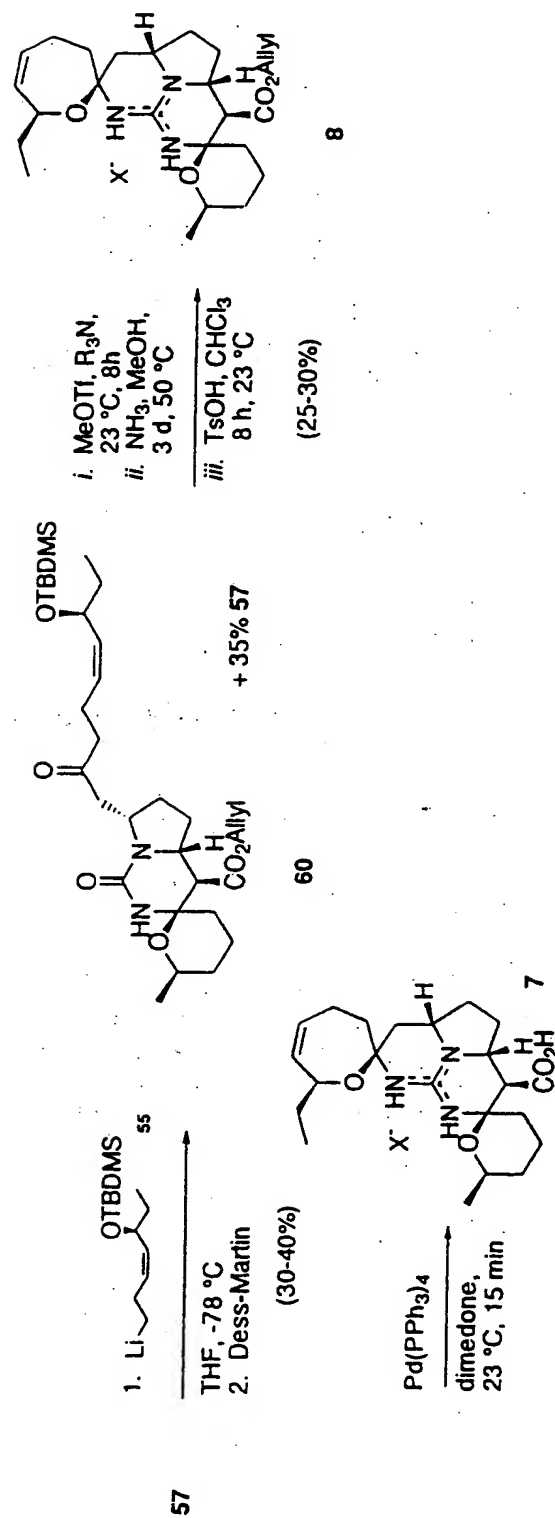


Figure 51

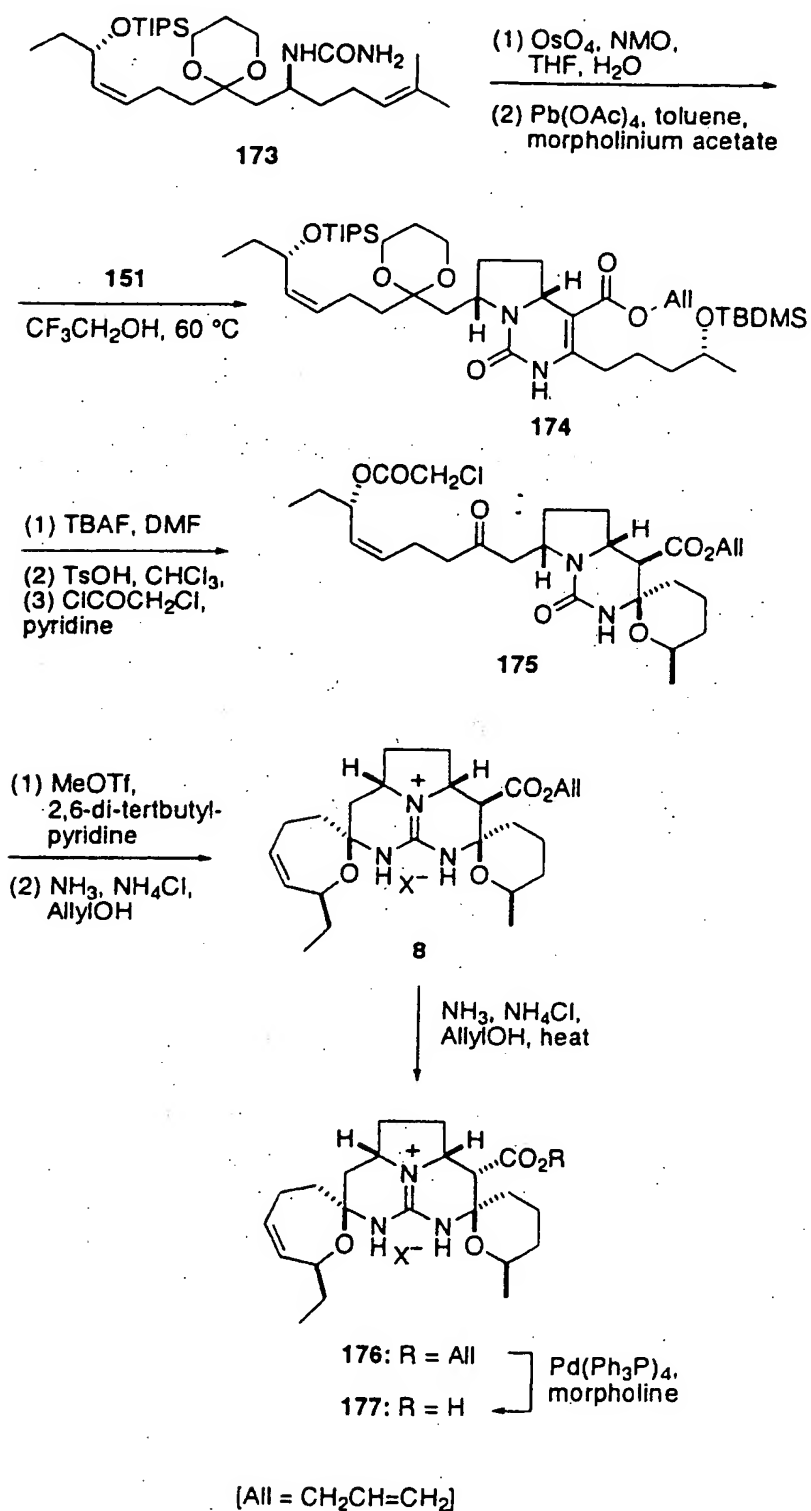


Figure 52

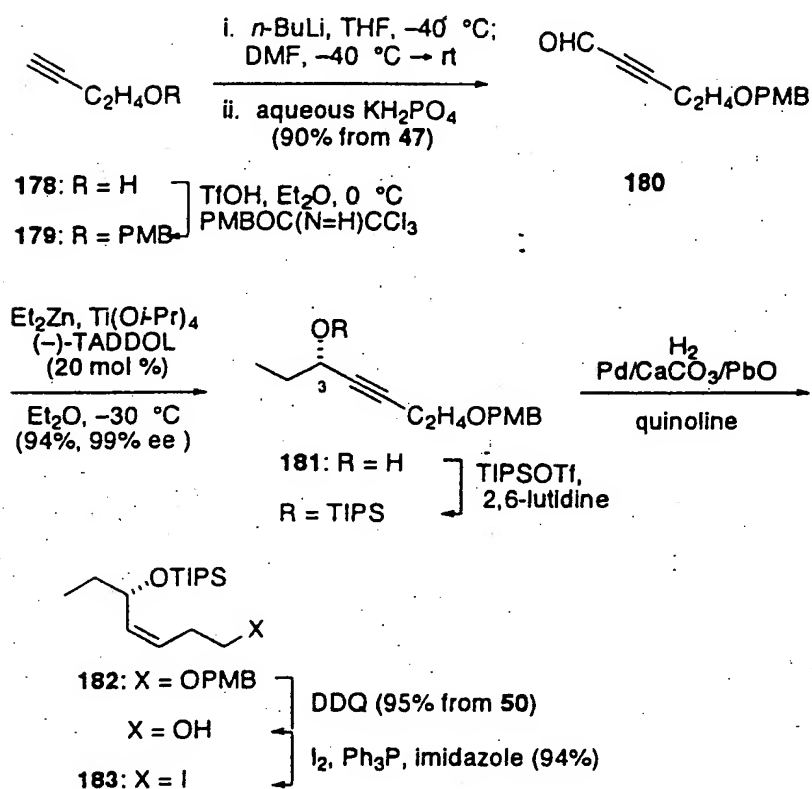


Figure 53

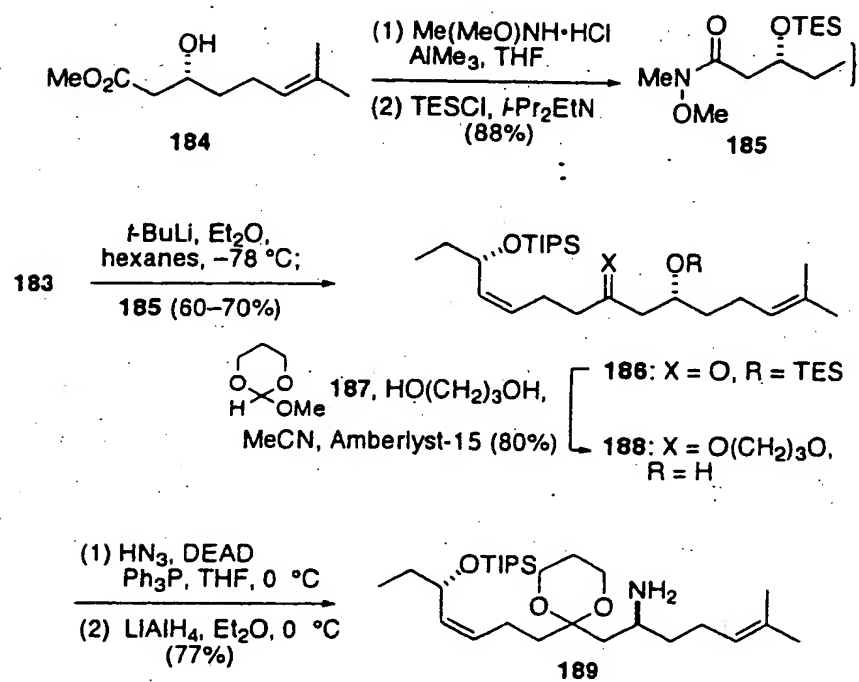


Figure 54

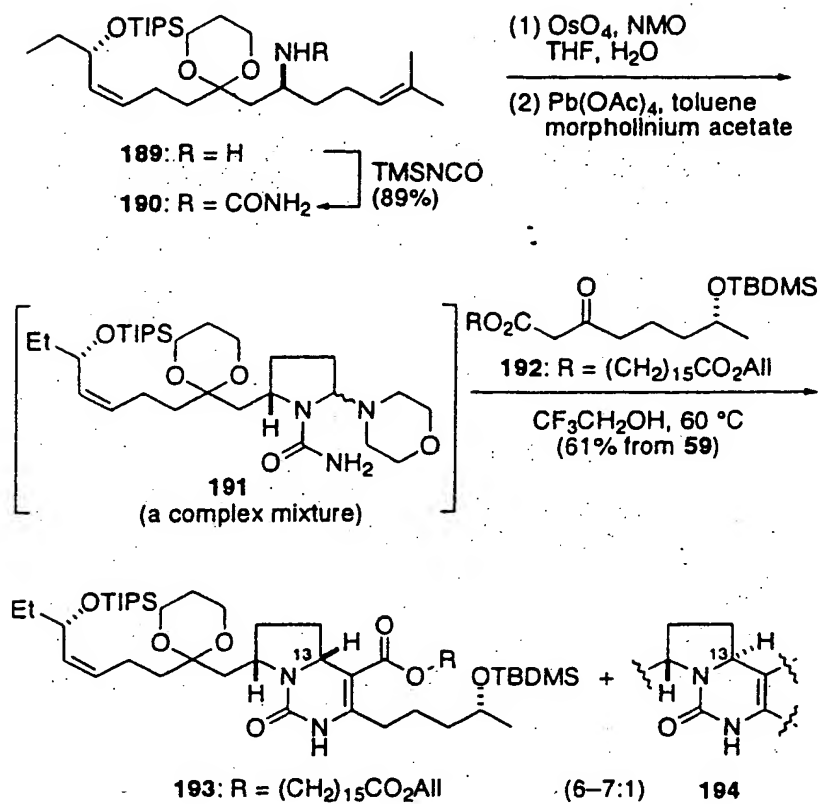


Figure 55

FIG. 56-A

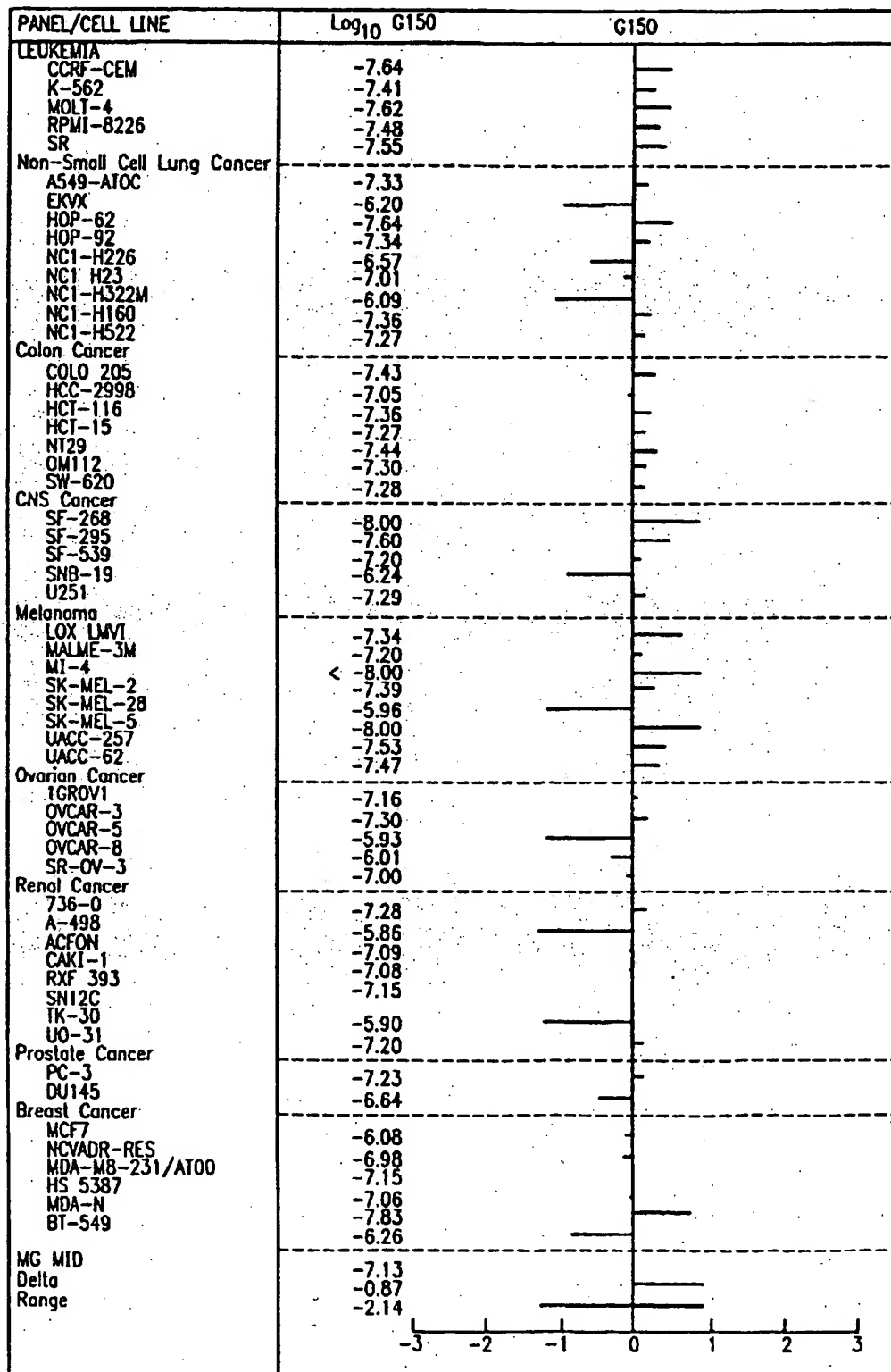


FIG. 56-B

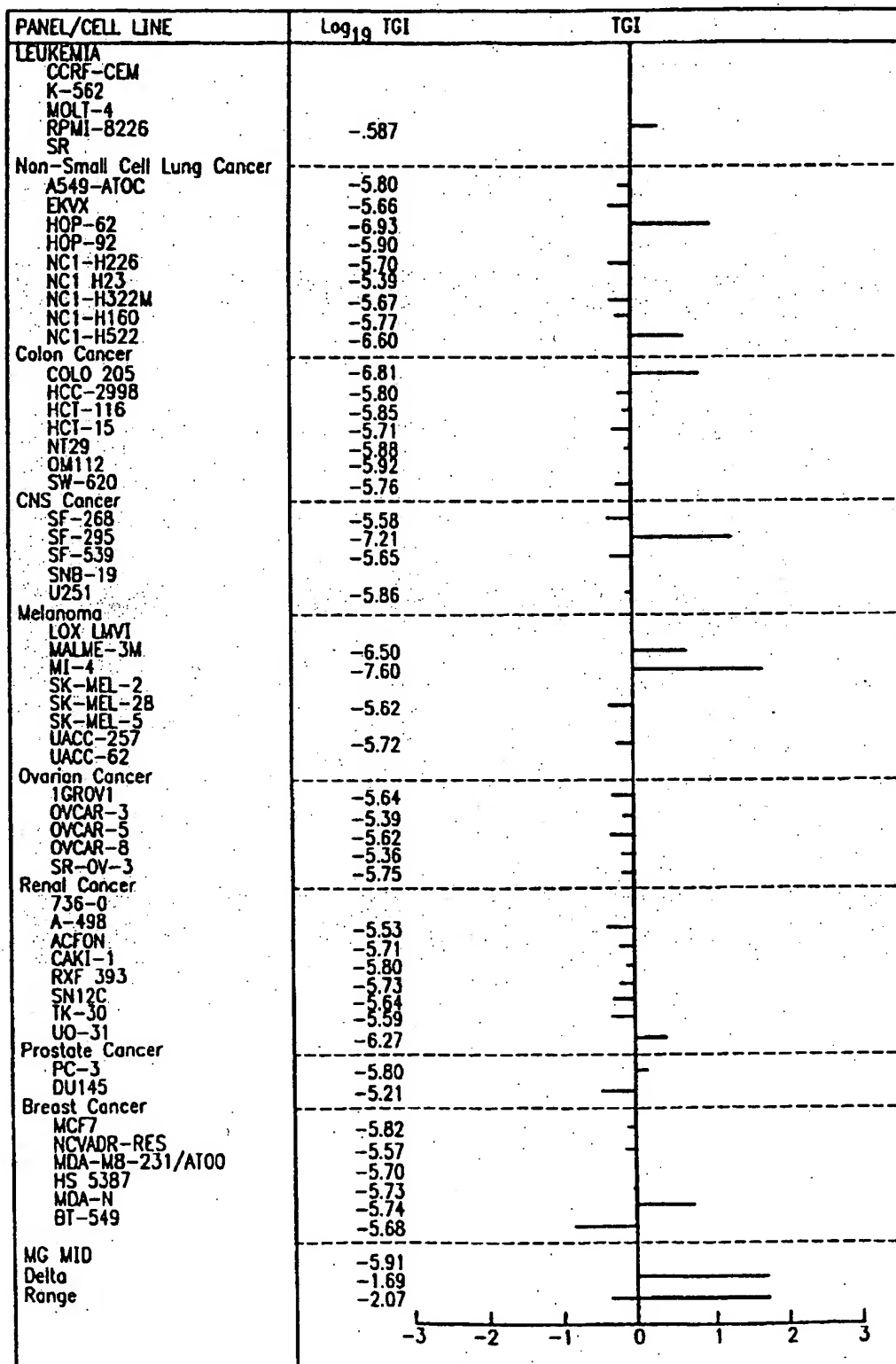


FIG. 56-C

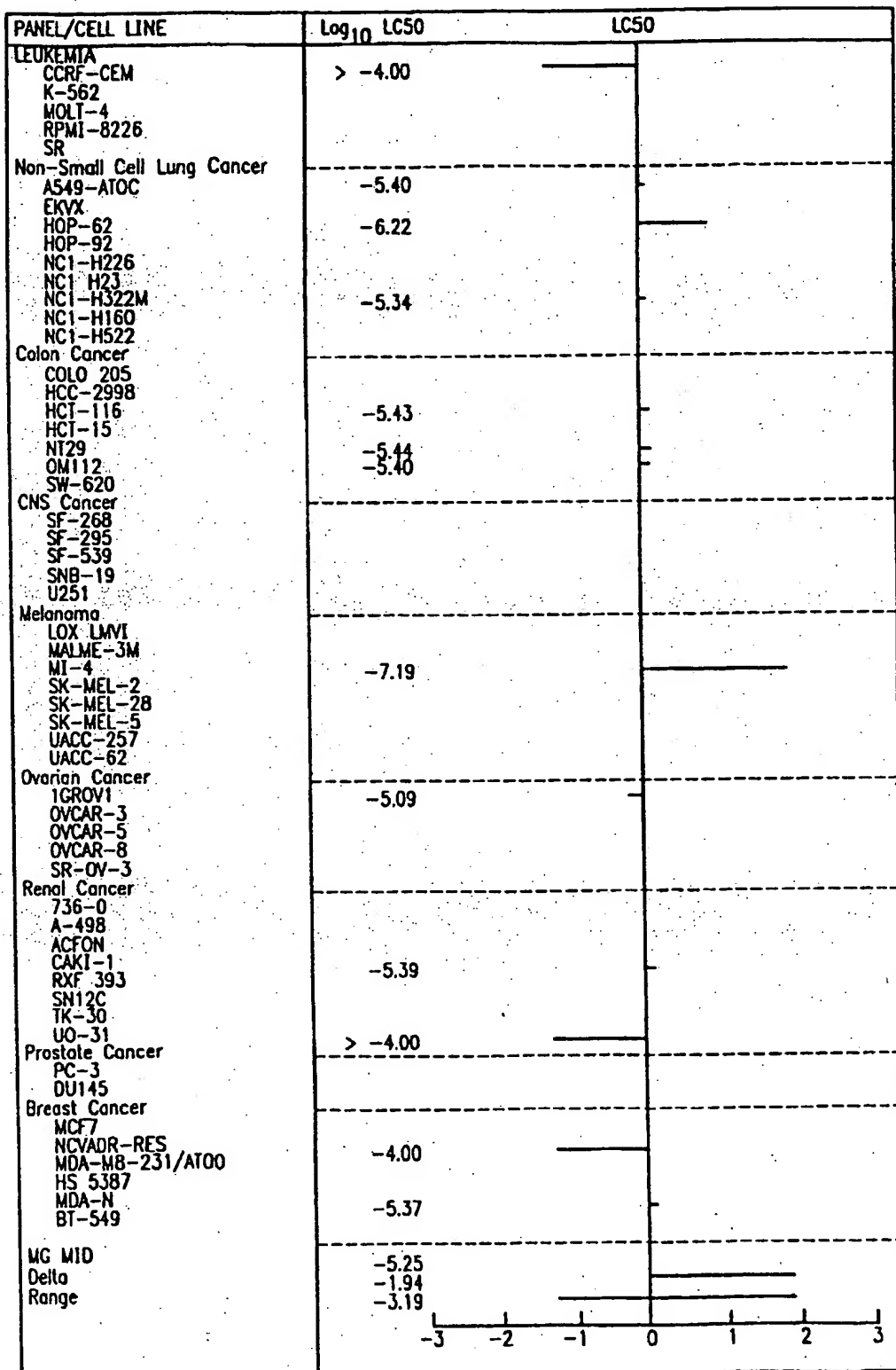


FIG. 57-A

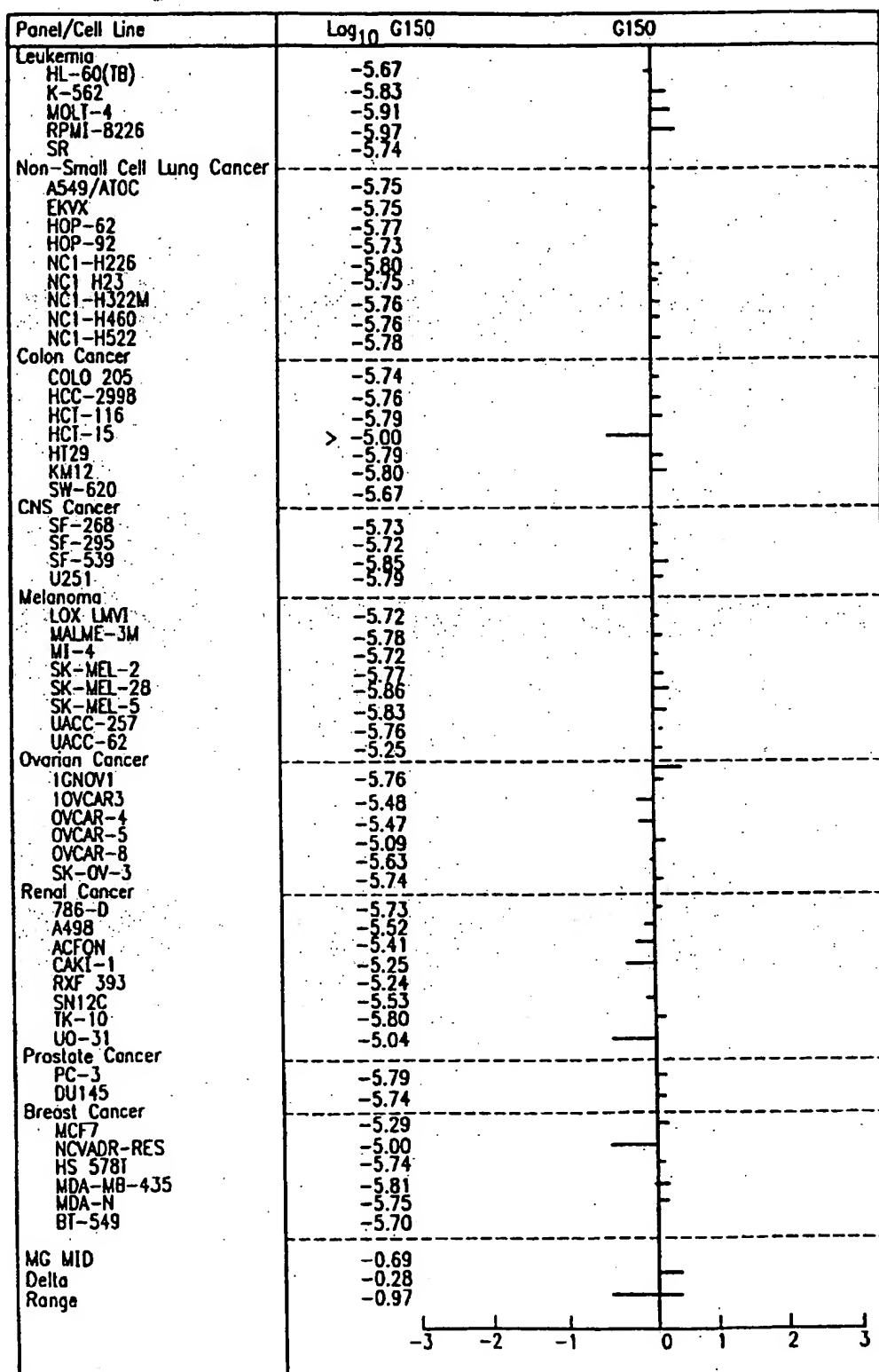


FIG. 57-B

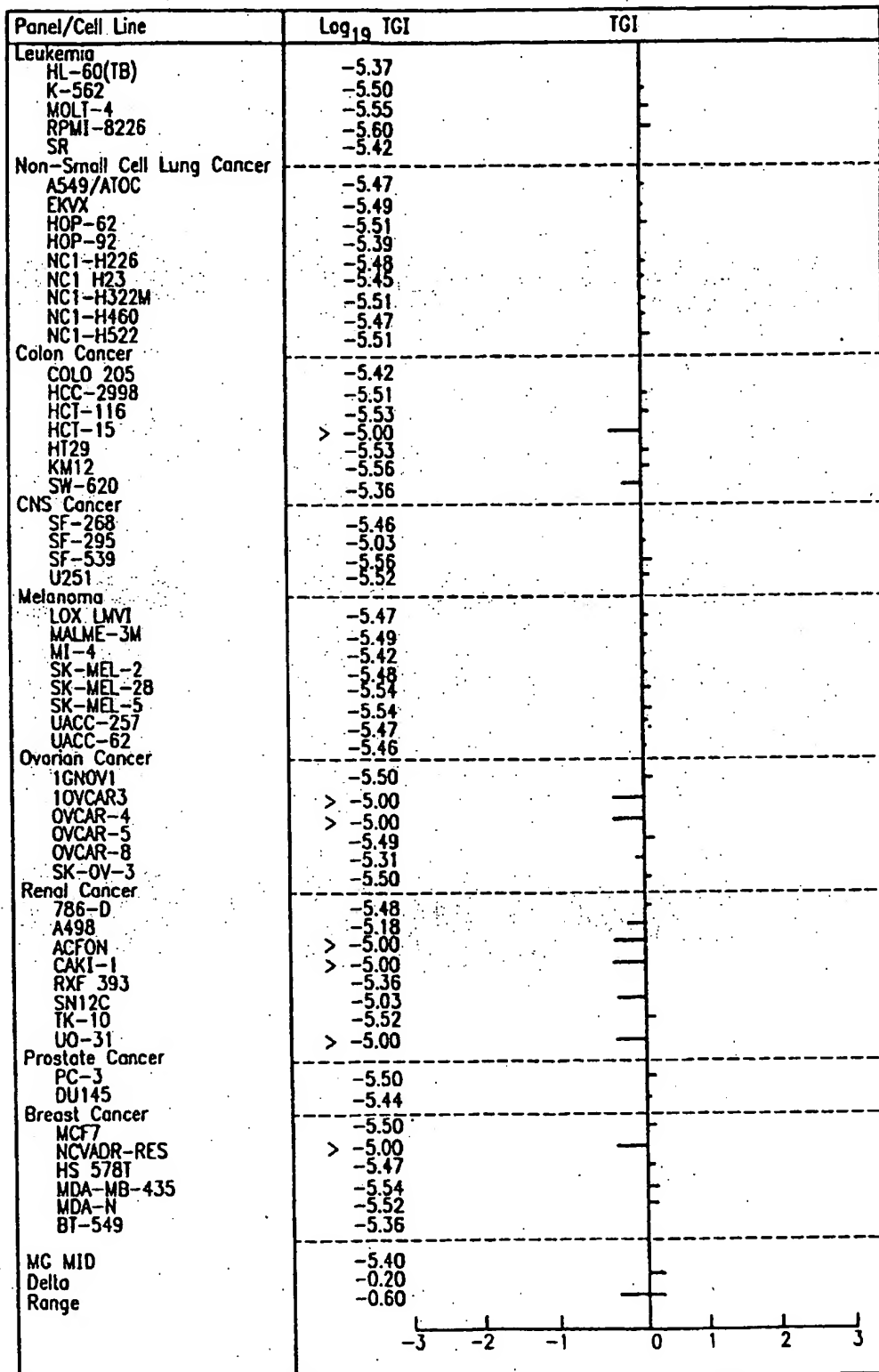


FIG. 57-C

Panel/Cell Line	Log ₁₀ LC50	LC50
Leukemia		
HL-60(TB)	-5.08	
K-562	-5.16	
MOLT-4	-5.19	
RPMI-8226	-5.22	
SR	-5.31	
Non-Small Cell Lung Cancer		
A549/ATOC	-5.20	
EKVX	-5.22	
HOP-62	-5.26	
HOP-92	-5.05	
NCI-H226	-5.16	
NCI-H23	-5.16	
NCI-H322M	-5.25	
NCI-H460	-5.19	
NCI-H522	-5.24	
Colon Cancer		
COLO 205	-5.30	
HCC-2998	-5.25	
HCT-116	-5.26	
HCT-15	> -5.00	
HT29	-5.26	
KM12	-5.27	
SW-620	> -5.00	
CNS Cancer		
SF-268	-5.20	
SF-295	-5.15	
SF-539	-5.26	
U251	-5.25	
Melanoma		
LOX LMVI	-5.23	
MALME-3M	-5.20	
M1-4	-5.12	
SK-MEL-2	-5.20	
SK-MEL-28	-5.22	
SK-MEL-5	-5.25	
UACC-257	-5.18	
UACC-62	-5.16	
Ovarian Cancer		
IGNOV1	-5.25	
1OVCAR3	> -5.00	
OVCAR-4	> -5.00	
OVCAR-5	-5.20	
OVCAR-8	> -5.00	
SK-OV-3	-5.25	
Renal Cancer		
786-D	-5.24	
A498	> -5.00	
ACFON	> -5.00	
CAKI-1	> -5.00	
RXF 393	> -5.00	
SN12C	> -5.00	
TK-10	-5.23	
UO-31	> -5.00	
Prostate Cancer		
PC-3	-5.23	
DU145	-5.14	
Breast Cancer		
MCF7	-5.23	
NCVADR-RES	> -5.00	
HS 578T	-5.20	
MDA-MB-435	-5.27	
MDA-N	-5.26	
BT-549	-5.02	
MG MID	-5.16	
Delta	-0.11	
Range	-0.27	

-3 -2 -1 0 1 2 3

FIG. 58-A

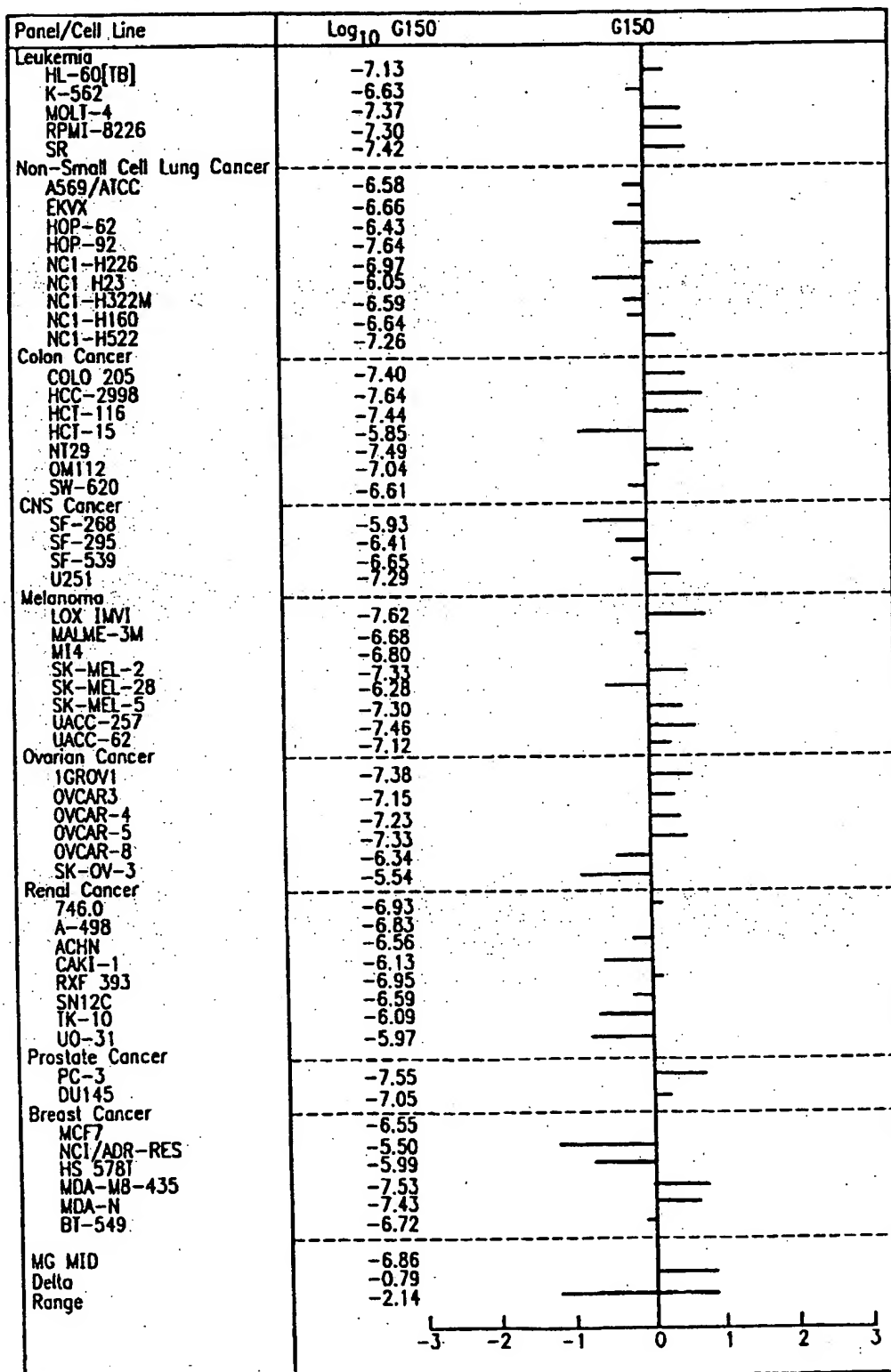


FIG. 58-B

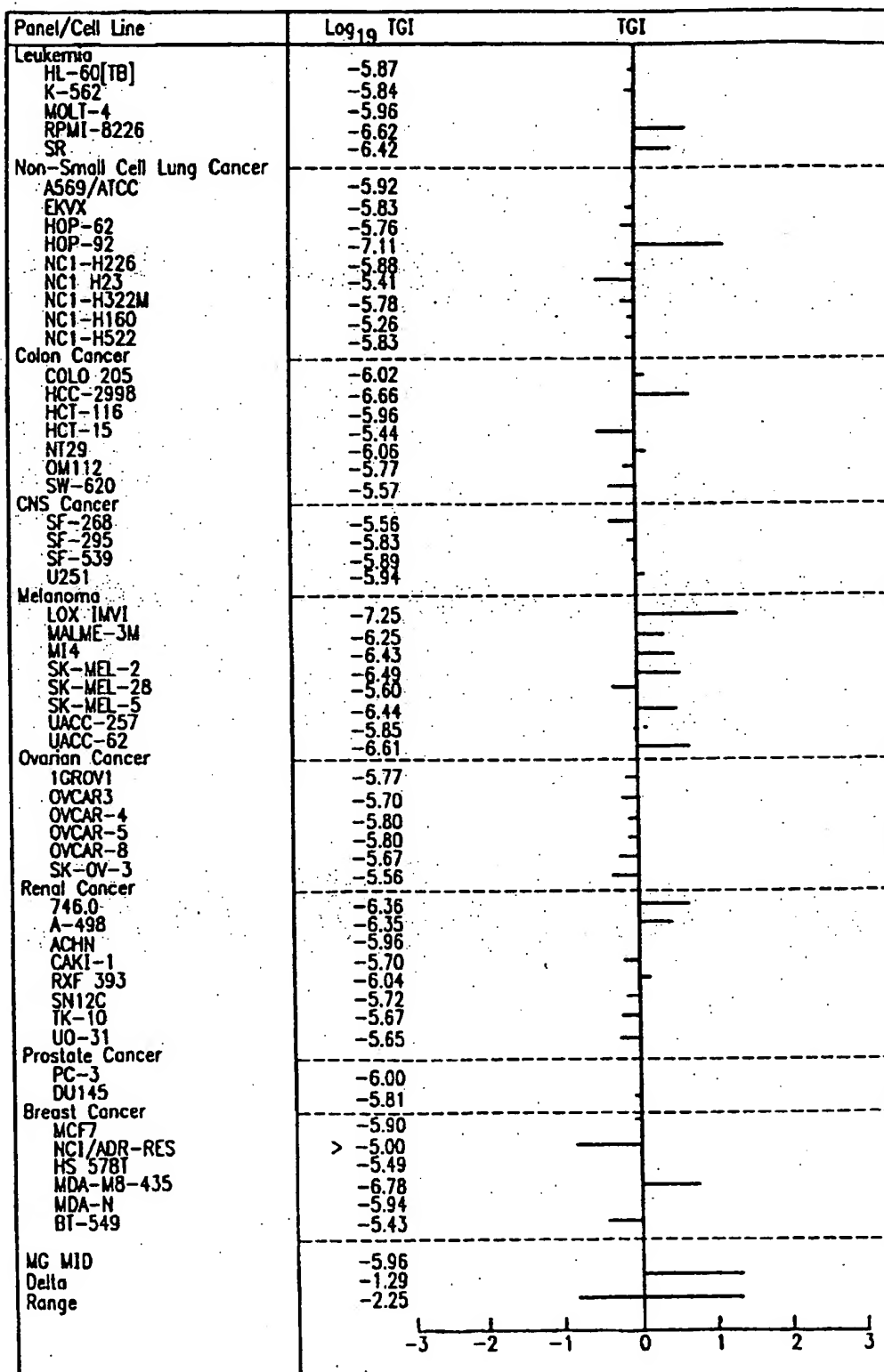


FIG. 58-C

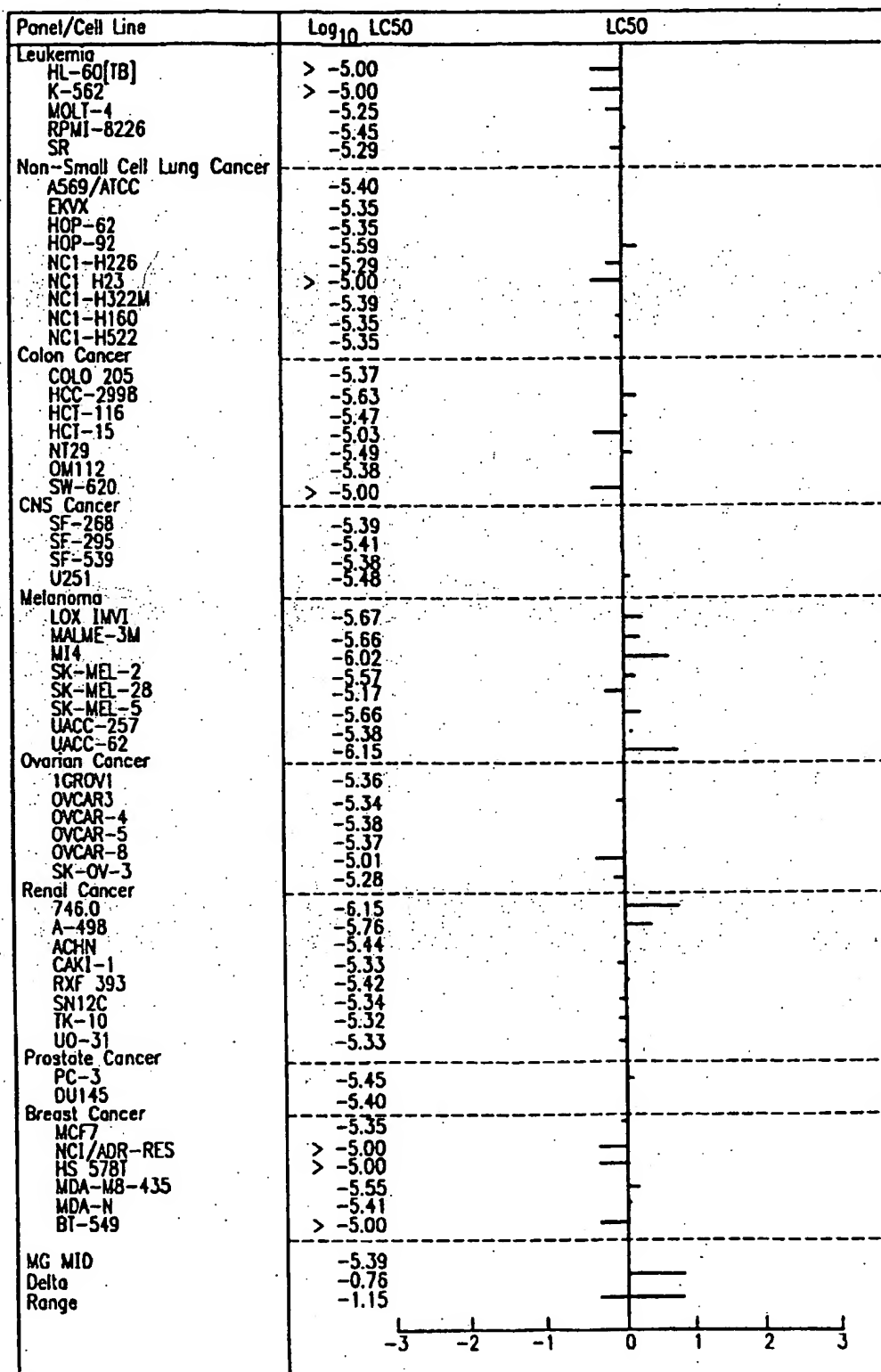


FIG. 59-A

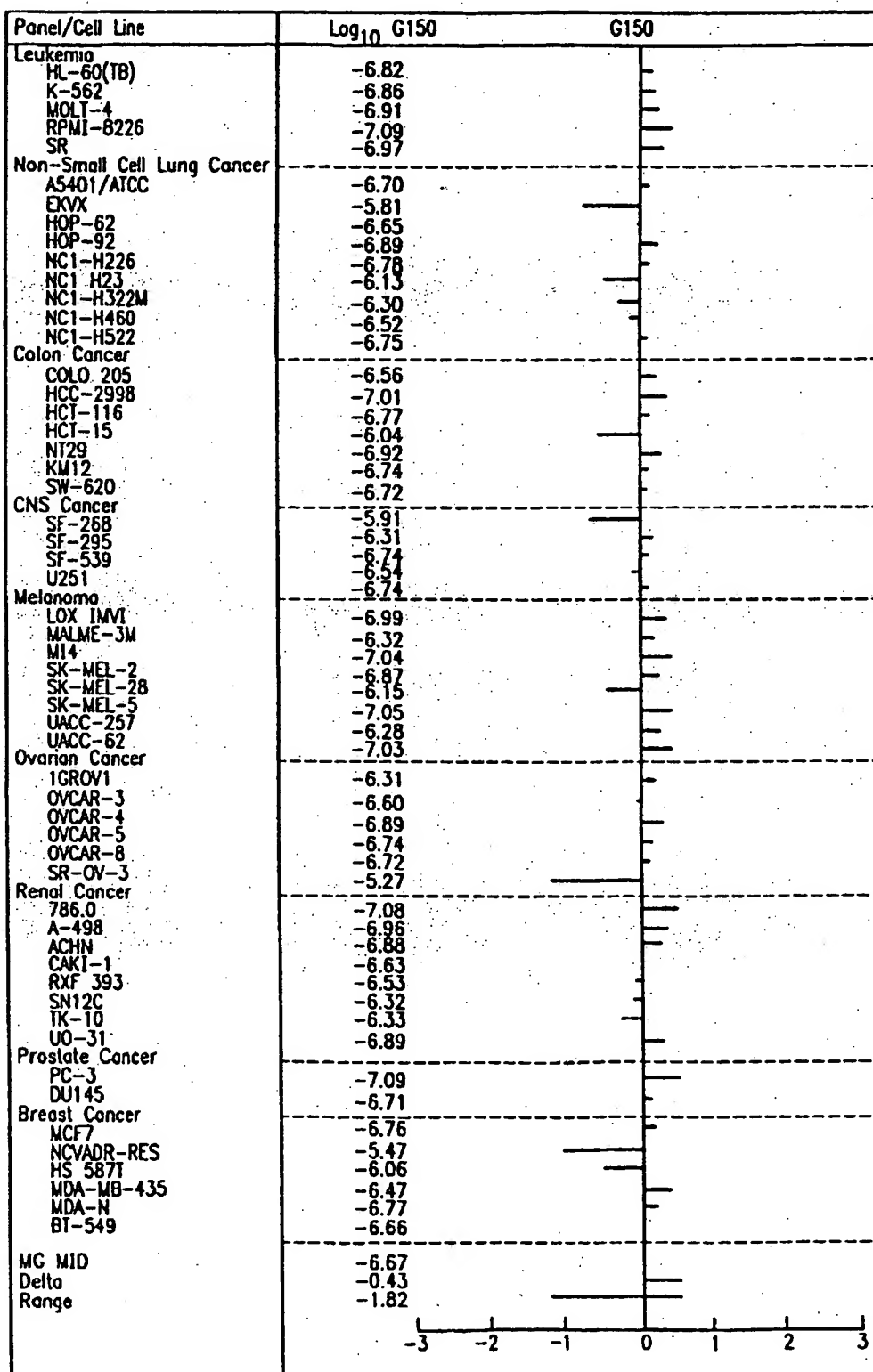


FIG. 59-B

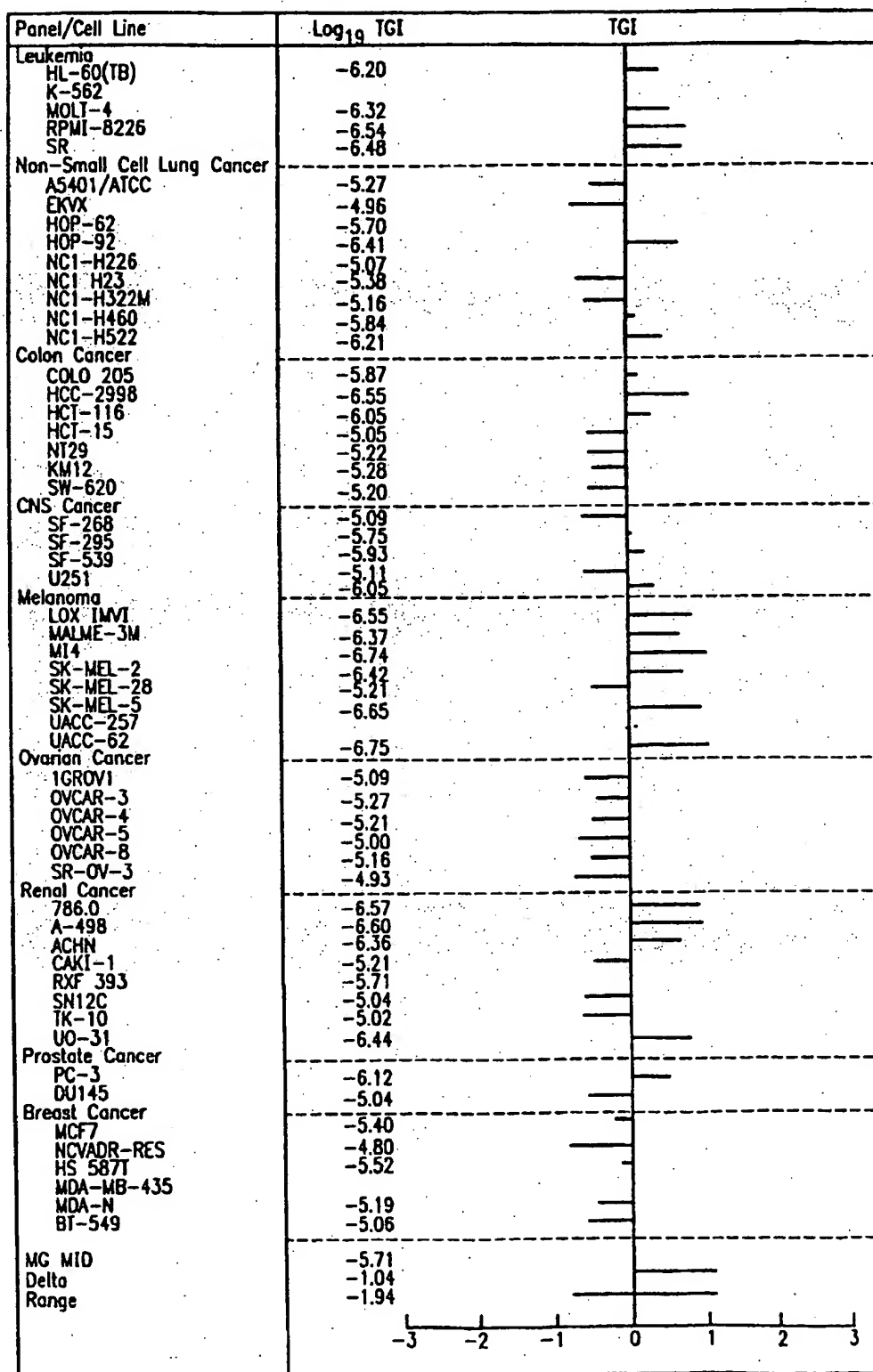


FIG. 59-C

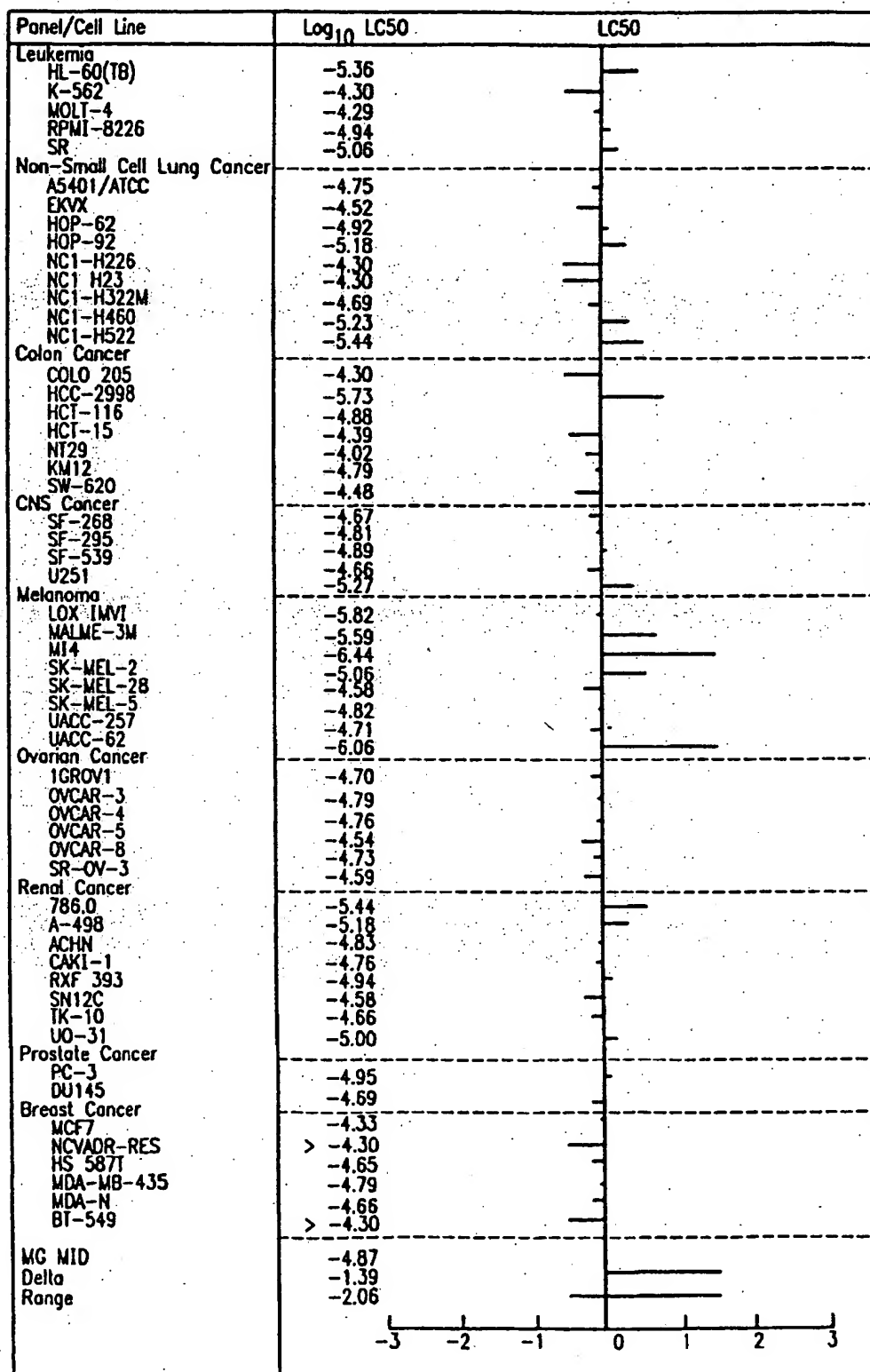


FIG. 60-A

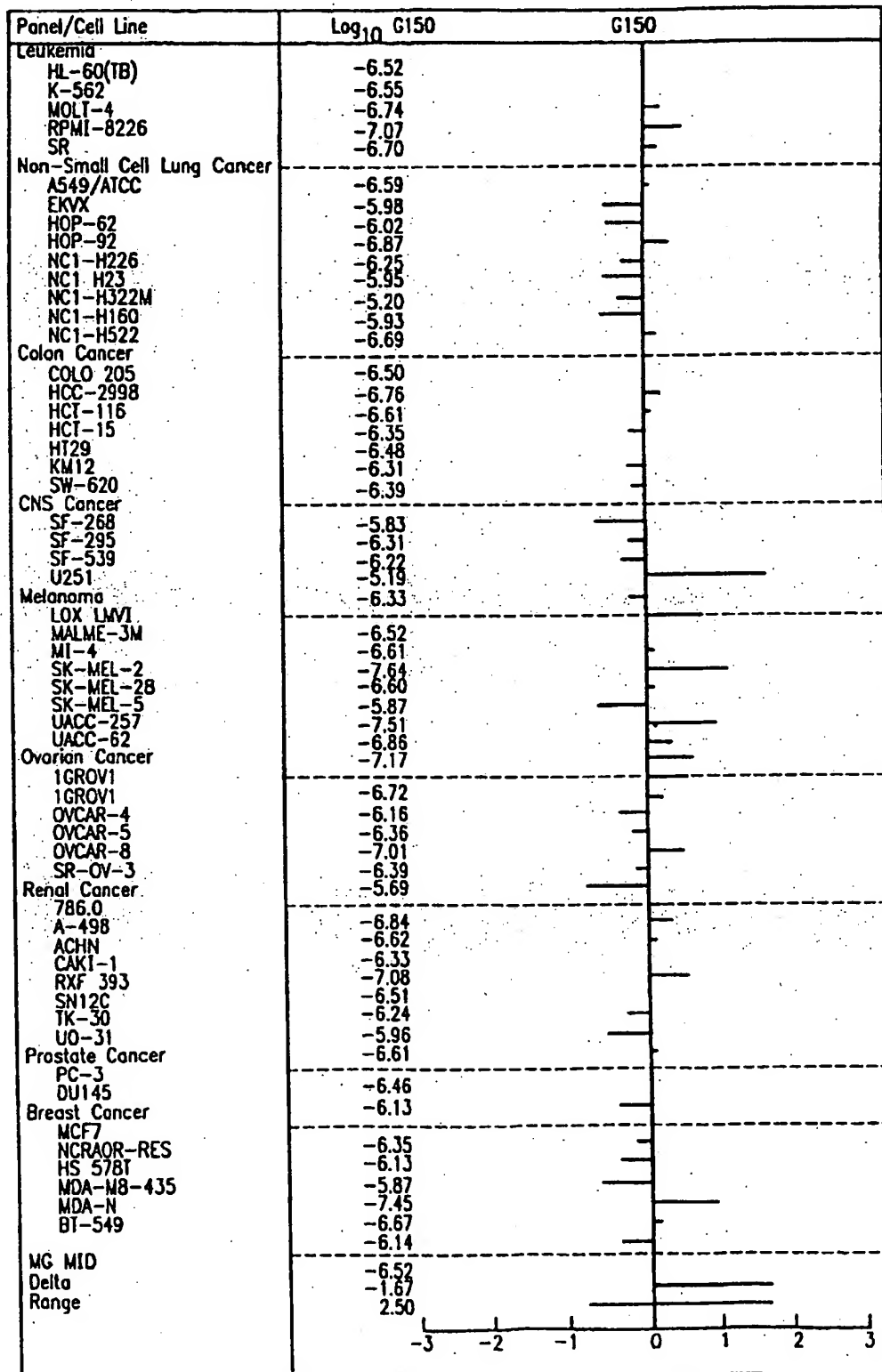


FIG. 60-B

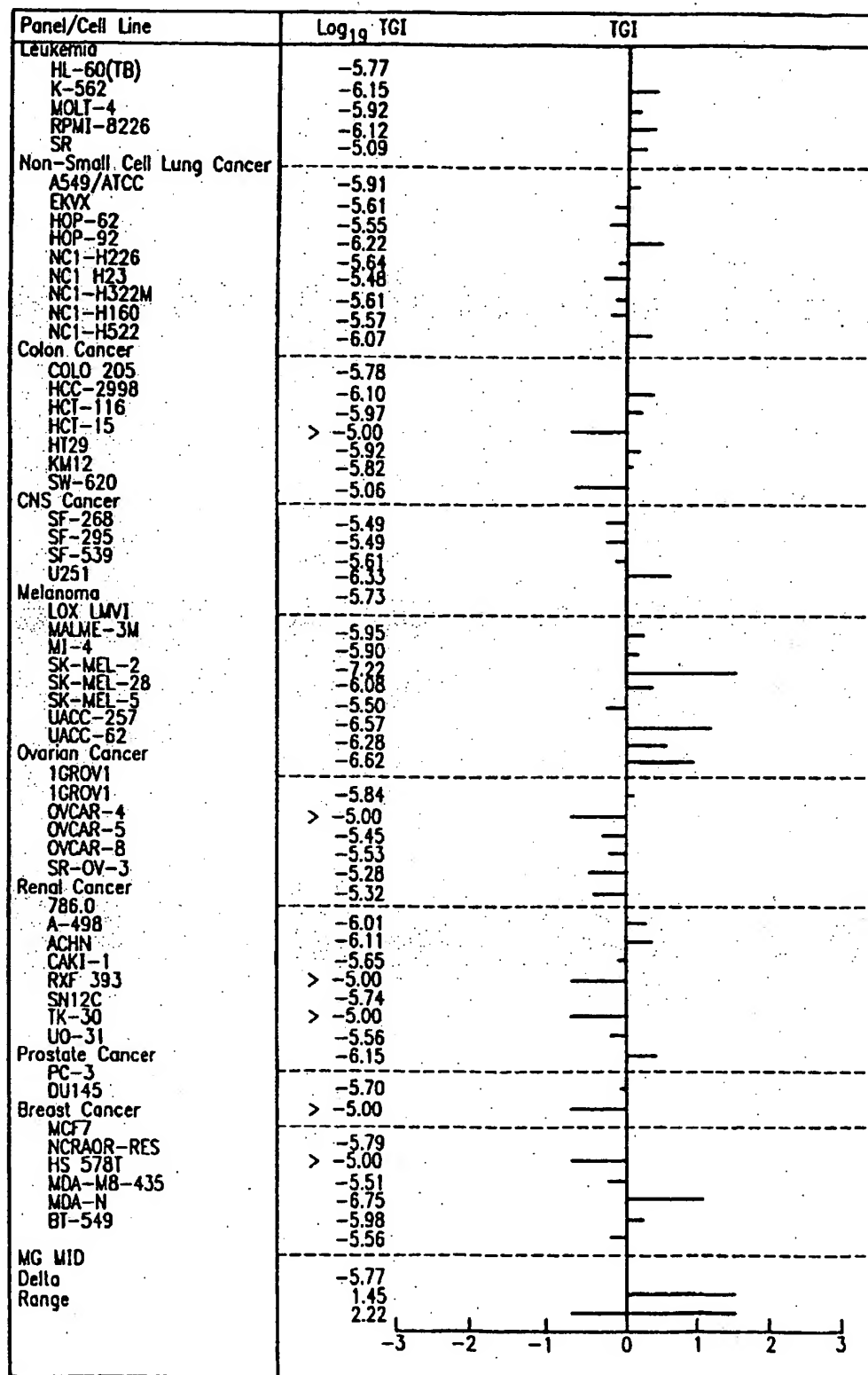


FIG. 60-C

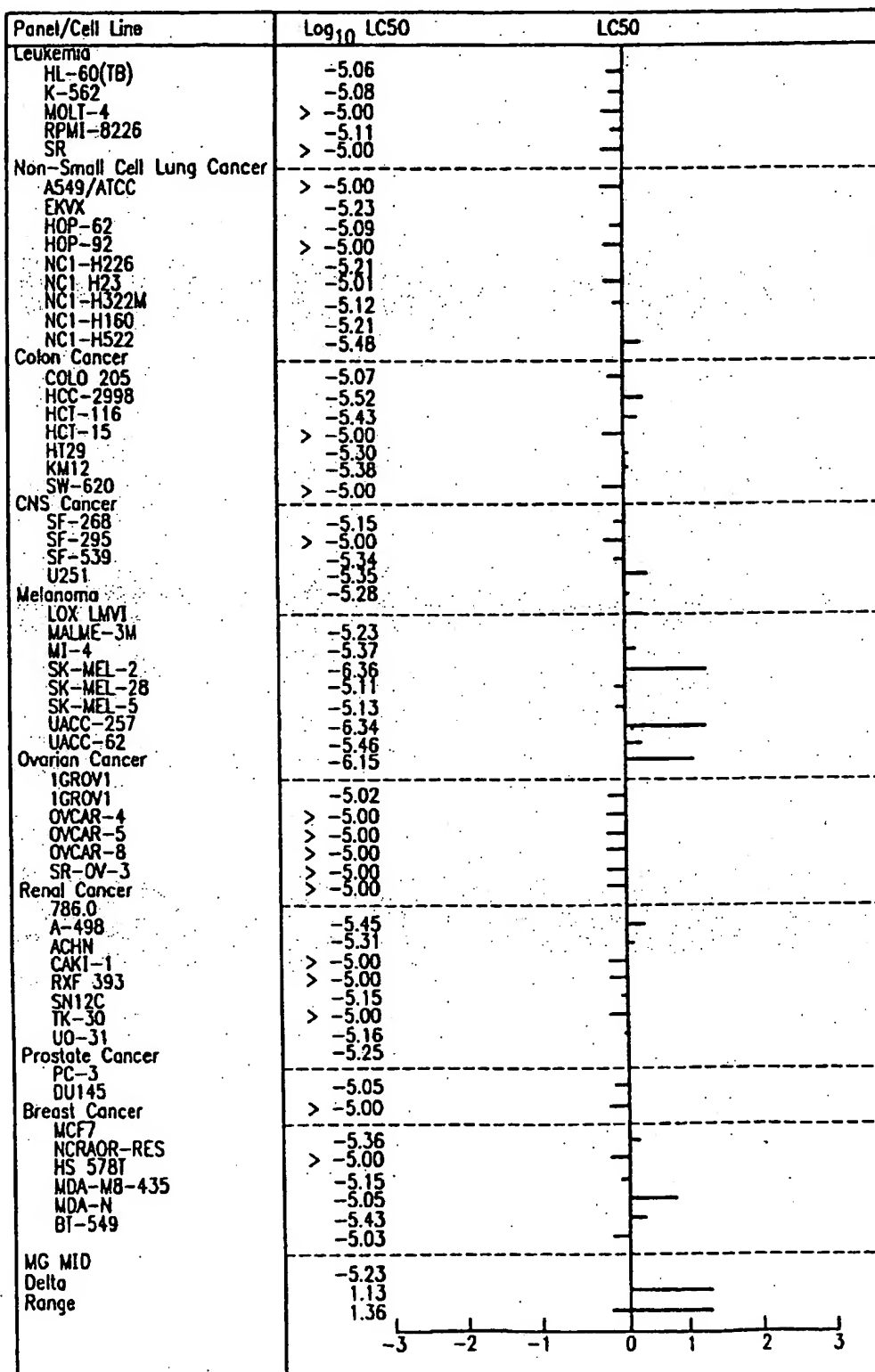


FIG. 61-A

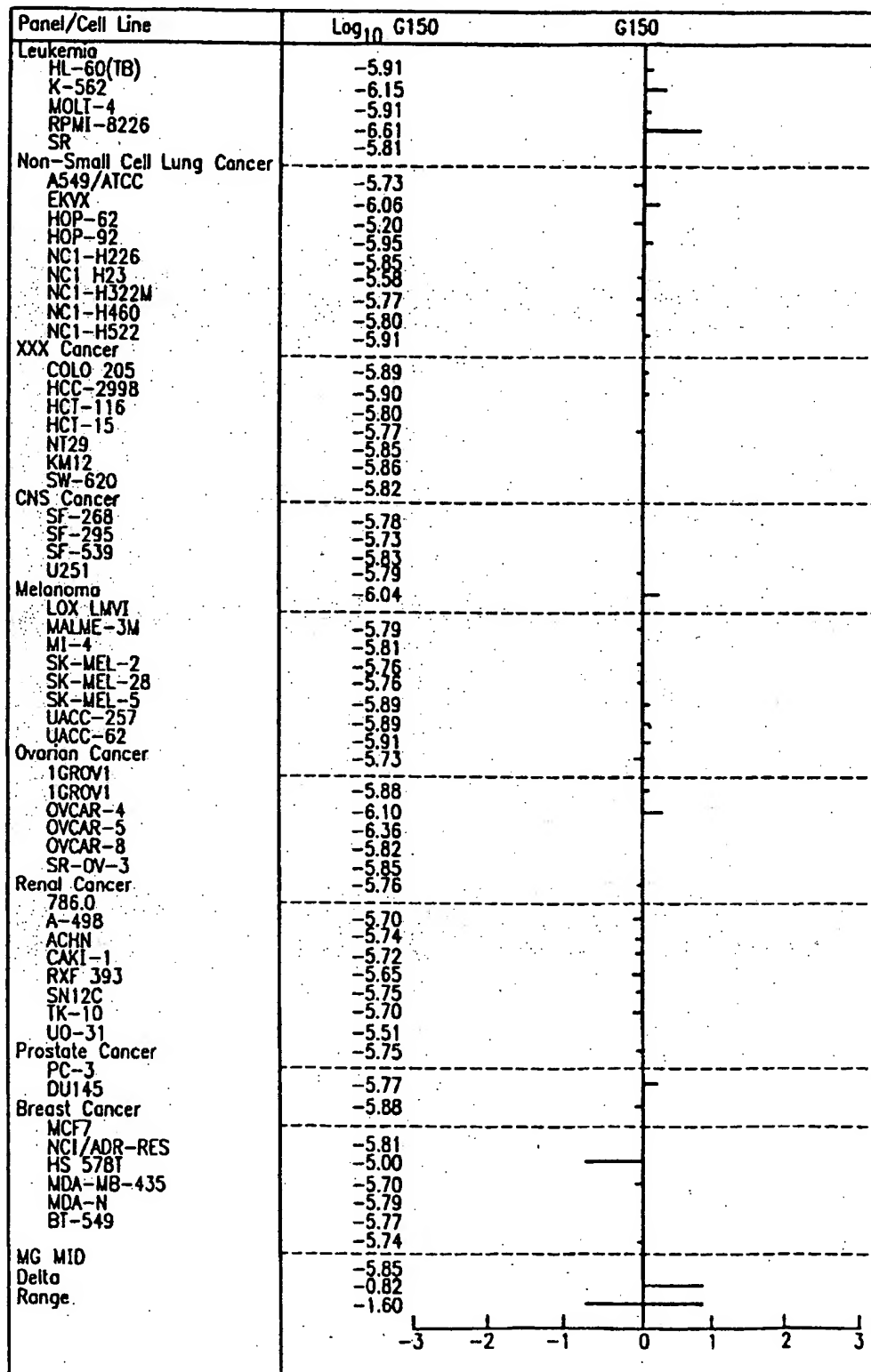


FIG. 61-B

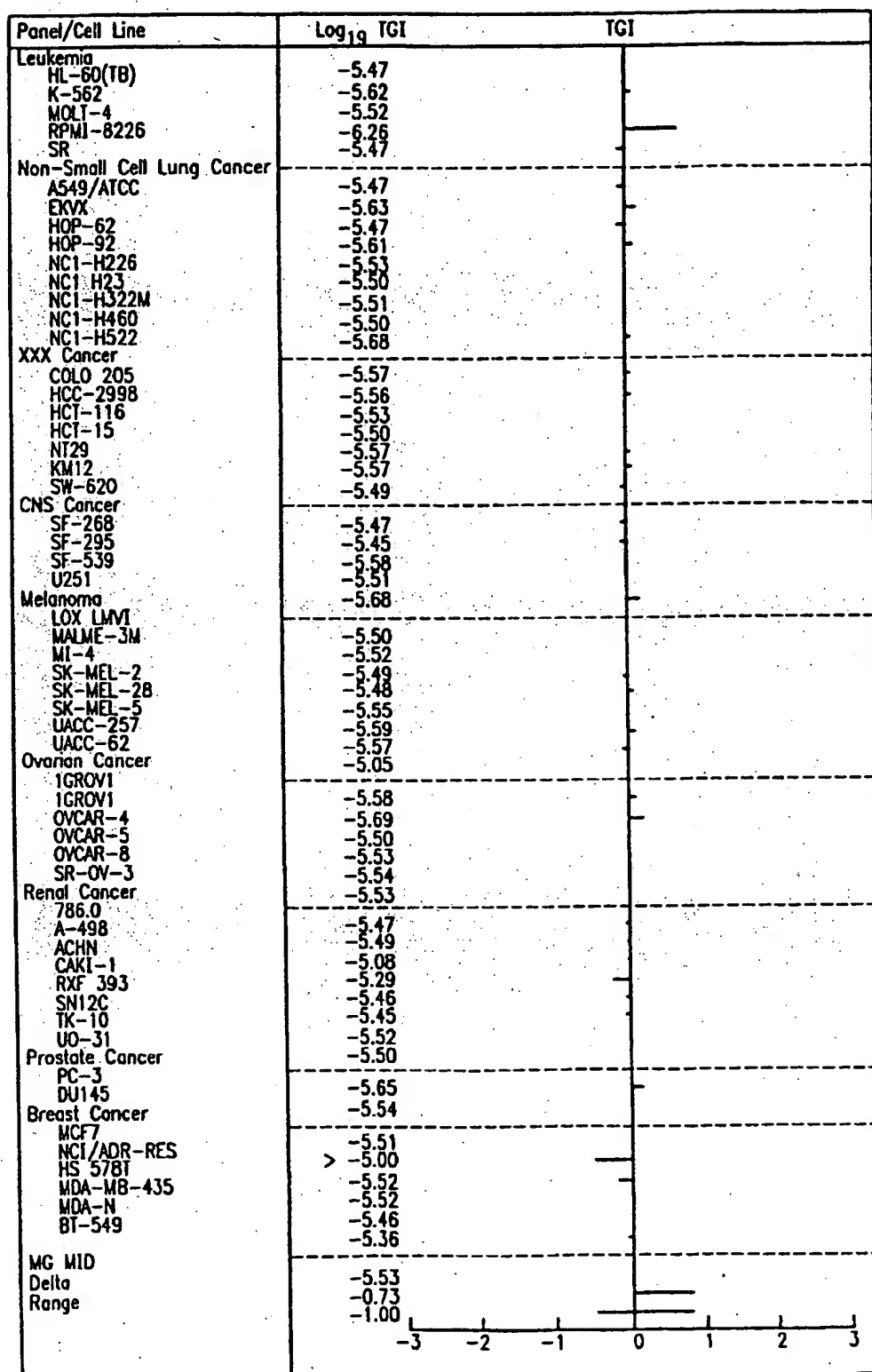


FIG. 61-C

Panel/Cell Line	Log ₁₀ LC50	LC50
Leukemia		
HL-60(TB)	-5.33	
K-562	-5.36	
MOLT-4	-5.14	
RPMI-8226	-5.34	
SR	-5.10	
Non-Small Cell Lung Cancer		
A549/ATCC	-5.21	
EKVX	-5.33	
HOP-62	-5.23	
HOP-92	-5.27	
NCI-H226	-5.21	
NCI H23	-5.19	
NCI-H322M	-5.26	
NCI-H460	-5.18	
NCI-H522	-5.25	
XXX Cancer		
COLO 205	-5.25	
HCC-2998	-5.27	
HCT-116	-5.27	
HCT-15	-5.21	
NT29	-5.23	
KM12	-5.28	
SW-620	-5.16	
CNS Cancer		
SF-268	-5.16	
SF-295	-5.23	
SF-539	-5.25	
U251	-5.24	
Melanoma		
LOX LMVI	-5.33	
MALME-3M	-5.22	
MT-4	-5.24	
SK-MEL-2	-5.22	
SK-MEL-28	-5.19	
SK-MEL-5	-5.27	
UACC-257	-5.29	
UACC-62	-5.24	
Ovarian Cancer		
IGROV1	-5.18	
IGROV1	-5.27	
OVCAR-4	-5.35	
OVCAR-5	-5.15	
OVCAR-8	-5.24	
SR-OV-3	-5.22	
Renal Cancer		
786.0	-5.25	
A-498	-5.23	
ACHN	-5.23	
CAKI-1	-5.24	
RXF 393	> -5.00	
SN12C	-5.18	
TK-10	-5.21	
UO-31	-5.24	
Prostate Cancer		
PC-3	-5.25	
DU145	-5.32	
Breast Cancer		
MCF7	-5.27	
NCI/ADR-RES	-5.21	
HS 578T	> -5.00	
MDA-MB-435	> -5.00	
MDA-N	-5.26	
BT-549	-5.26	
MG MID		
Delta	-5.17	
Range	-5.22	
	-0.10	
	-0.39	

-3 -2 -1 0 1 2 3

FIG. 62-A

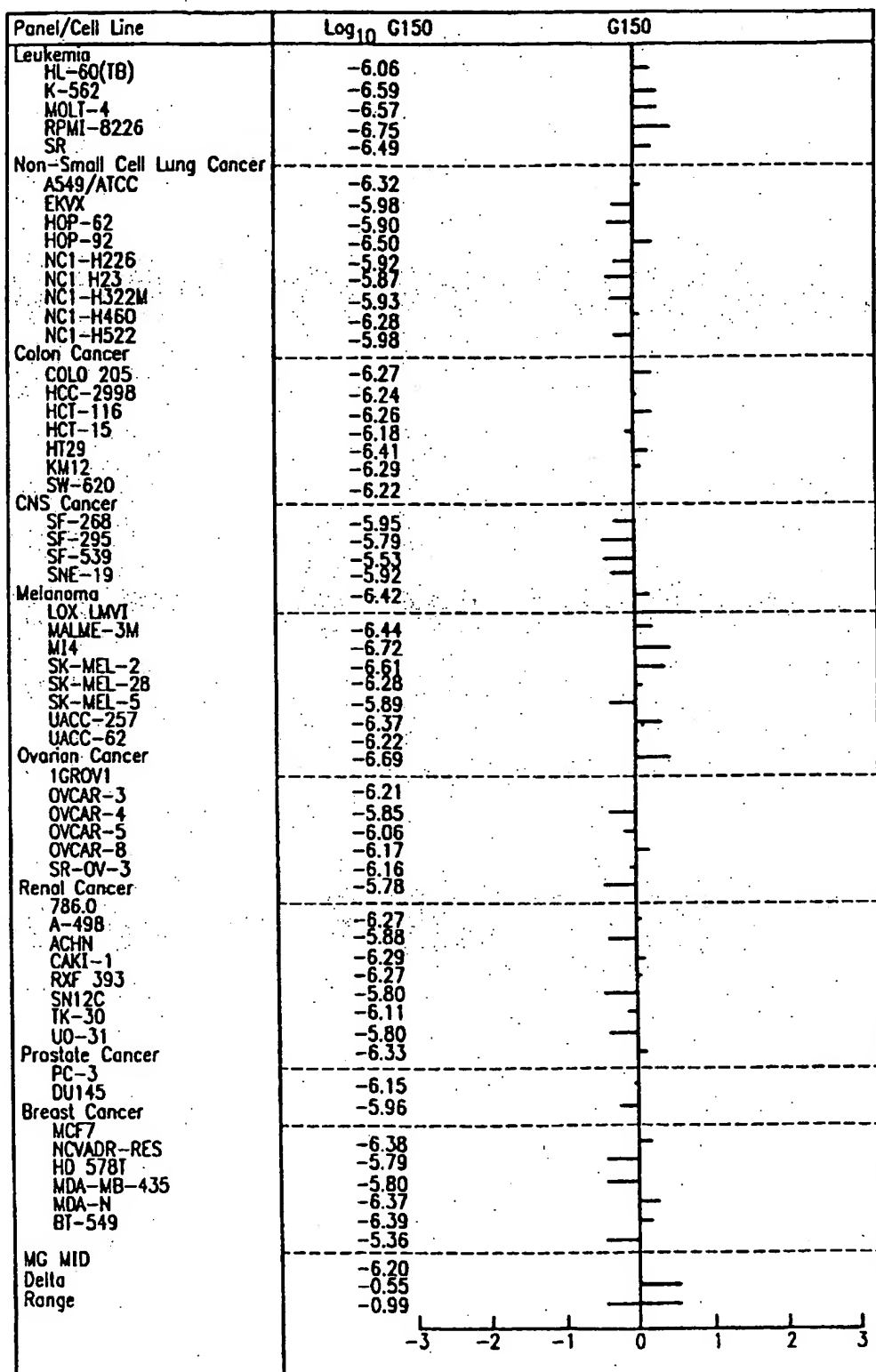


FIG. 62-B

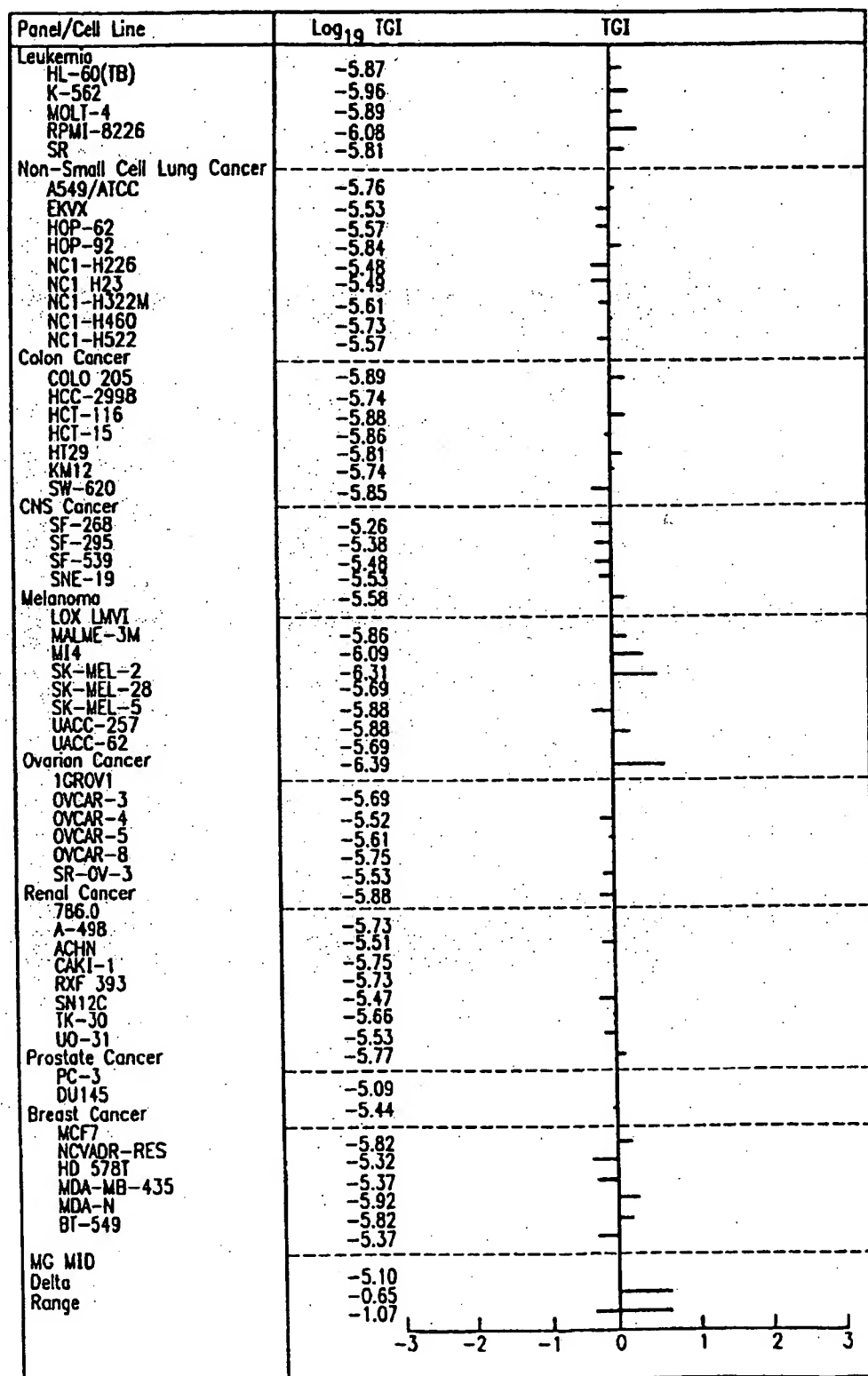


FIG. 62-C

